UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-Q

(Mark One)

x QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Quarterly Period Ended March 31, 2008

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number 0-19125

Isis Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**33-0336973**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

1896 Rutherford Road, Carlsbad, CA 92008
(Address of principal executive offices, including zip code)

760-931-9200
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act: **None**

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $.001 Par Value

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definition of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer x
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12(b)-2 of the Securities Exchange Act of 1934). Yes o No x

The number of shares of voting common stock outstanding as of May 5, 2008 was 95,383,770.

ISIS PHARMACEUTICALS, INC.
FORM 10-Q

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TRADEMARKS

Isis Pharmaceuticals® is a registered trademark of Isis Pharmaceuticals, Inc.
Ibis Biosciences™ is a trademark of Ibis Biosciences, Inc.
Ibis T5000™ is a trademark of Ibis Biosciences, Inc.
Regulus Therapeutics™ is a trademark of Regulus Therapeutics LLC.
Vitravene® is a registered trademark of Novartis AG.

ISIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share data)

	March 31, 2008 (Unaudited)	December 31, 2007
ASSETS		
Current assets:		
Cash and cash equivalents	$ 271,936	$ 138,614
Short-term investments	66,479	55,105
Contracts receivable	4,358	6,177
Inventories	3,700	2,817
Other current assets	6,378	4,604
Total current assets	352,851	207,317
Property, plant and equipment, net	8,274	7,131
Licenses, net	18,516	19,100
Patents, net	18,390	17,759
Debt issuance costs	4,539	4,740
Deposits and other assets	2,854	2,811
Total assets	$ 405,424	$ 258,858
LIABILITIES AND STOCKHOLDERS' EQUITY		

Current liabilities:		
Accounts payable	$ 5,633	$ 4,507
Accrued compensation	2,449	10,461
Accrued liabilities	5,301	6,794
Derivative instruments related to Abbott's subscription right and call option	3,455	—
Current portion of long-term obligations	5,471	7,238
Current portion of deferred contract revenue	57,951	33,205
Total current liabilities	80,260	62,205
2[5]¤8% convertible subordinated notes	162,500	162,500
Long-term obligations, less current portion	391	362
Long-term deferred contract revenue	84,798	23,548
Total liabilities	327,949	248,615
Noncontrolling interest in Regulus Therapeutics LLC	8,488	9,371
Noncontrolling interest in Ibis Biosciences, Inc.	14,366	—
Stockholders' equity:		
Common stock, $0.001 par value; 200,000,000 shares authorized, 92,994,635 and 87,239,423 shares issued and outstanding at March 31, 2008 and December 31, 2007, respectively	93	87
Additional paid-in capital	884,434	827,992
Accumulated other comprehensive income	2,123	538
Accumulated deficit	(832,029)	(827,745)
Total stockholders' equity	54,621	872
Total liabilities, noncontrolling interest and stockholders' equity	$ 405,424	$ 258,858

See accompanying notes

ISIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except for per share amounts)
(Unaudited)

	Three Months Ended March 31,	
	2008	2007
Revenue:		
Research and development revenue under collaborative agreements	$ 20,686	$ 2,002
Licensing and royalty revenue	668	448
Total revenue	21,354	2,450
Expenses:		
Research and development	26,449	19,949
Selling, general and administrative	3,736	3,402
Total operating expenses	30,185	23,351
Loss from operations	(8,831)	(20,901)
Other income (expense):		
Investment income	4,956	3,401
Interest expense	(1,398)	(2,628)
Gain on investments	—	1,521
Loss on early retirement of debt	—	(1,219)
Loss attributed to noncontrolling interest in Symphony GenIsis, Inc.	—	6,806
Loss attributed to noncontrolling interest in Regulus Therapeutics LLC	883	—
Loss attributed to noncontrolling interest in Ibis Biosciences, Inc.	105	—
Net loss applicable to common stock	$ (4,285)	$ (13,020)
Basic and diluted net loss per share	$ (0.05)	$ (0.16)
Shares used in computing basic and diluted net loss per share	90,799	82,456

See accompanying notes.

ISIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)
(Unaudited)

	Three Months Ended March 31,	
	2008	2007
Net cash provided by (used in) operating activities	$ 75,114	$ (20,795)
Investing activities:		
Purchases of short-term investments	(73,921)	(47,493)
Proceeds from the sale of short-term investments	62,635	24,481
Purchases of property, plant and equipment	(1,373)	(539)
Acquisition of licenses and other assets	(84)	(354)
Proceeds from the sale of strategic investments	—	2,245
Net cash used in investing activities	(12,743)	(21,660)
Financing activities:		
Net proceeds from issuance of equity	2,727	1,188
Proceeds from issuance of 2[5]¤8% convertible subordinated notes, net of issuance costs	—	157,067
Principal and redemption premium payment on prepayment of the $5^1/_2$% convertible subordinated notes	—	(44,926)
Principal payments on debt and capital lease obligations	(1,738)	(1,965)
Proceeds from stock purchase by Genzyme Corporation, net of fees	49,962	—
Proceeds from capital contribution to Ibis Biosciences, Inc.	20,000	—
Net cash provided by financing activities	70,951	111,364
Net increase in cash and cash equivalents	133,322	68,909
Cash and cash equivalents at beginning of period	138,614	114,514
Cash and cash equivalents at end of period	$ 271,936	$ 183,423
Supplemental disclosures of cash flow information:		
Interest paid	$ 2,244	$ 860
Supplemental disclosures of non-cash investing and financing activities:		
Amounts accrued for capital and patent expenditures	$ 1,372	$ 443

See accompanying notes.

ISIS PHARMACEUTICALS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
March 31, 2008
(Unaudited)

1. Basis of Presentation

The unaudited interim condensed consolidated financial statements for the three month periods ended March 31, 2008 and 2007 have been prepared on the same basis as the audited financial statements for the year ended December 31, 2007. The financial statements include all normal recurring adjustments, which we consider necessary for a fair presentation of the financial position at such dates and the operating results and cash flows for those periods. Results for the interim periods are not necessarily indicative of the results for the entire year. For more complete financial information, these financial statements, and notes thereto, should be read in conjunction with the audited financial statements for the year ended December 31, 2007 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission ("SEC").

The condensed consolidated financial statements include the accounts of Isis Pharmaceuticals, Inc. ("we", "us" or "our"), our wholly owned subsidiaries, Isis Pharmaceuticals Singapore Pte Ltd., Isis USA Ltd. and Symphony GenIsis, Inc. In addition to our wholly owned subsidiaries, our condensed consolidated financial statements include two variable interest entities, Ibis Biosciences, Inc. and Regulus Therapeutics LLC, for which we are the primary beneficiary as defined by Financial Accounting Standards Board Interpretation ("FIN") 46R (revised 2003), *Consolidation of Variable Interest Entities, an Interpretation of ARB 51*. All significant intercompany balances and transactions have been eliminated.

2. Significant Accounting Policies

Revenue recognition

We follow the provisions as set forth by Staff Accounting Bulletin ("SAB") 101, *Revenue Recognition in Financial Statements*, SAB 104, *Revenue Recognition*, and Financial Accounting Standards Board Emerging Issues Task Force ("EITF") 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*.

We generally recognize revenue when we have satisfied all contractual obligations and are reasonably assured of collecting the resulting receivable. We are often entitled to bill our customers and receive payment from our customers in advance of recognizing the revenue under current accounting rules. In those instances where we have received payment from our customers in advance of recognizing revenue, the amounts are included in deferred revenue on the consolidated balance sheet.

Research and development revenue under collaborative agreements

We often enter into collaborations where we receive non-refundable upfront payments for prior or future expenditures. We recognize revenue related to upfront payments ratably over our period of performance relating to the term of the contractual arrangements. Occasionally, we are required to estimate our period of performance when the agreements we enter into do not clearly define such information. Should different estimates prevail, revenue recognized could be materially different. To date our estimates have not required material adjustments. We have made estimates of our continuing obligations on several agreements. Our collaborative agreements typically include a research and/or development project plan that includes activities to be performed during the collaboration and the party responsible for performing them. We estimate the period of time over which we will complete the activities for which we are responsible and use that period of time as our period of performance for purposes of revenue recognition and amortize revenue over such period. When our collaborators have asked us to continue performing work in a collaboration beyond the initial period of performance, we have extended our amortization period to correspond to the new extended period of performance. In no case have adjustments to date to performance periods and related adjustments to revenue amortization periods had a material impact on our revenue.

Our collaborations often include contractual milestones. When we achieve these milestones, we are entitled to payment, as defined by the underlying agreements. We generally recognize revenue related to milestone payments upon completion of the milestone's substantive performance requirement, as long as we are reasonably assured of collecting the resulting receivable and we are not obligated for future performance related to the achievement of the milestone.

We generally recognize revenue related to the sale of our drug inventory as we ship or deliver drugs to our partners. In several instances, we completed the manufacturing of drugs, but our partners asked us to deliver the drug on a later date. Under these circumstances, we ensured that the provisions in SAB 104 were met before we recognized the related revenue.

We often enter into revenue arrangements that contain multiple deliverables. In these cases, we recognize revenue from each element of the arrangement as long as we are able to determine a separate fair value for each element, we have completed our obligation to deliver or perform on that element and we are reasonably assured of collecting the resulting receivable.

In the fourth quarter of 2006, we started to sell the Ibis T5000 Biosensor System commercially. The sale of each Ibis T5000 Biosensor System contains multiple elements. Since we had no previous experience commercially selling the Ibis T5000 Biosensor System, we had no basis to determine the fair values of the various elements included in each system; therefore, we account for the entire system as one deliverable and recognize revenue over the period of performance. The assay kits, which are sold separately from the instrument, are considered part of the system from an accounting perspective because the assay kits and the instrument are dependent on each other. For a one-year period following the sale, we have ongoing support obligations for the Ibis T5000 Biosensor System; therefore, we are amortizing the revenue for the entire system, including related assay kits, over a one-year period. Once we obtain a sufficient number of sales to enable us to identify each element's fair value, we will be able to recognize revenue separately for each element.

As part of our Genzyme strategic alliance, in February 2008 Genzyme Corporation made a $150 million equity investment by purchasing 5 million shares of common stock at $30 per share. The price Genzyme paid for our common stock represented a significant premium over the fair value of our stock. Using a Black-Scholes option valuation model, we determined that the value of the premium was $100 million, which represents value Genzyme gave to us to help fund the companies' research collaboration which began in January 2008. We accounted for this premium as deferred revenue and are amortizing it into revenue over the four year period of our performance beginning in the first quarter of 2008.

Licensing and royalty revenue

We often enter into agreements to license our proprietary patent rights on an exclusive or non-exclusive basis in exchange for license fees and/or royalties. We generally recognize as revenue immediately those licensing fees and royalties for which we have no future significant performance obligations and are reasonably assured of collecting the resulting receivable.

Short-term investments

We have equity investments in privately- and publicly-held biotechnology companies. We hold ownership interests of less than 20% in each of the respective entities. In determining if and when a decrease in market value below our cost in our equity positions is temporary or other-than-temporary, we examine historical trends in the stock price, the financial condition of the issuer, near term prospects of the issuer and our current need for cash. Unrealized gains and losses related to temporary declines are recorded as a separate component of stockholders' equity. When we determine that a decline in value is other-than-temporary, we recognize an impairment loss in the period in which the other-than-temporary decline occurs. We determined that there were no other-than-temporary declines in value of our investments during the three months ended March 31, 2008 and 2007. During the first quarter of 2007, we sold a portion of the equity securities of Alnylam Pharmaceuticals, Inc. that we owned resulting in a realized gain of $1.5 million.

Inventory valuation

In accordance with Statement of Financial Accounting Standards ("SFAS") 2, *Accounting for Research and Development Costs*, we capitalize the costs of raw materials that we purchase for use in producing our drugs because until we use these raw materials they have alternative future uses. We include in inventory raw material costs and related manufacturing costs for drugs that we manufacture for our partners under contractual terms and that we use primarily in our clinical development activities and drug products. Each of our raw materials can be used in multiple products and, as a result, has future economic value independent of the development status of any single drug. For example, if one of our drugs failed, the raw materials allocated for that drug could be used to manufacture our other drugs. We expense these costs when we deliver the drugs to our partners, or as we provide these drugs for our own clinical trials. Also included in inventory are material costs, labor costs and manufacturing overhead costs associated with the Ibis T5000 Biosensor System and related assay kits. We reflect our inventory on the balance sheet at the lower of cost or market value under the first-in, first-out method. We review inventory periodically and reduce the carrying value of items considered to be slow moving or obsolete to their estimated net realizable value. We consider several factors in estimating the net realizable value, including shelf life of raw materials, alternative uses for our drugs and clinical trial materials and historical write-offs. We did not record any inventory write-offs during the first three months of 2008 and 2007.

Total inventory includes the following as of March 31, 2008 and December 31, 2007 (in thousands):

	March 31, 2008	December 31, 2007
Raw materials	$ 3,449	$ 2,679
Work-in-process	251	138
	$ 3,700	$ 2,817

Patents

We capitalize costs consisting principally of outside legal costs and filing fees related to obtaining patents. We review our capitalized patent costs regularly to determine that they include costs for patent applications that have future value. We evaluate costs related to patents that we are not actively pursuing and write off any of these costs, if appropriate. We amortize patent costs over their estimated useful lives of ten years, beginning with the date the patents are issued. For the first quarter of 2008 and 2007, we recorded a non-cash charge of $98,000 and $168,000, respectively, which was included in research and development expenses and was related to the write-down of our patent costs to their estimated net realizable values.

Long-lived assets

We assess the value of our long-lived assets, which include property, plant and equipment, patent costs, and licenses acquired from third parties, under the provisions set forth by SFAS 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, and we evaluate our long-lived assets for impairment on at least a quarterly basis.

Use of estimates

The preparation of condensed consolidated financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the condensed consolidated financial statements and accompanying notes. Actual results could differ from those estimates. Historically, our estimates have been accurate as we have not experienced any material differences between our estimates and our actual results.

Consolidation of variable interest entities

We have implemented the provisions of FIN 46R, which addresses consolidation by business enterprises of variable interest entities either: (1) that do not have sufficient equity investment at risk to permit the entity to finance its activities without additional subordinated financial support, or (2) in which the equity investors lack an essential characteristic of a controlling financial interest. As of March 31, 2008, we had collaborative arrangements with nine entities that we consider to be variable interest entities under FIN 46R. For the three months ended March 31, 2008, our condensed consolidated financial statements include two variable interest entities, Ibis and Regulus, for which we are the primary beneficiary.

Comprehensive loss

SFAS 130, *Reporting Comprehensive Income*, requires us to report, in addition to net loss, comprehensive loss and its components. A summary follows (in thousands):

	Three Months Ended March 31,	
	2008	2007
Comprehensive loss:		
Unrealized holding gains (losses)	$ 1,585	$ (780)
Reclassification adjustment for realized gains included in net income	—	(1,417)
Net loss applicable to common stock	(4,285)	(13,020)
Comprehensive loss	$ (2,700)	$ (15,217)

Stock-based compensation expense

We account for our stock-based compensation expense related to employee stock options and employee stock purchases under SFAS 123R, *Share-Based Payment*. We estimate the fair value of each stock option grant and the employee stock purchase plan ("ESPP") purchase rights on the date of grant using the Black-Scholes model. The expected term of stock options granted represents the period of time that they are expected to be outstanding. For the stock options granted subsequent to January 1, 2008, we estimated the expected term of options granted based on historical exercise patterns. For the stock options granted prior to January 1, 2008, the estimated expected term is a derived output of the simplified method, as allowed under SAB 107.

For the quarter ended March 31, 2008 and 2007, we used the following weighted-average assumptions in our Black-Scholes calculations:

Employee Stock Options:

	Three Months Ended March 31,	
	2008	2007
Risk-free interest rate	3.1%	4.7%
Dividend yield	0.0%	0.0%
Volatility	55.0%	63.8%
Expected Life	4.6 years	4.6 years

ESPP:

	Three Months Ended March 31,	
	2008	2007
Risk-free interest rate	3.3%	5.1%
Dividend yield	0.0%	0.0%
Volatility	56.7%	56.1%
Expected Life	6 months	6 months

We record stock options granted to non-employees, which consist primarily of options granted to Regulus' Scientific Advisory Board, at their fair value in accordance with the requirements of SFAS 123R, then periodically remeasure them in accordance with EITF 96-18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, and recognize the expense over the service period.

Stock-based compensation expense for the three months ended March 31, 2008 and 2007 (in thousands, except per share data) was allocated as follows:

	Three Months Ended March 31,	
	2008	2007
Research and development	$ 3,075	$ 1,926
Selling, general and administrative	684	438
Non-cash compensation expense related to stock options included in operating expenses	$ 3,759	$ 2,364
Basic and diluted net loss per share	$ (0.04)	$ (0.03)

As part of the Regulus joint venture, both we and Alnylam issued our own company's stock options to members of Regulus' Board of Directors and Scientific Advisory Board. The expense associated with these options are recorded on Regulus' books. Since we are consolidating the financial results of Regulus, $375,000 of non-cash stock based compensation expense associated with these options for the first quarter of 2008 is included in our consolidated expenses.

As of March 31, 2008, total unrecognized compensation cost related to non-vested stock-based compensation plans was $21.1 million. Total unrecognized compensation cost will be adjusted for future changes in estimated forfeitures. We expect to recognize this cost over a weighted average period of 1.5 years.

Impact of recently issued accounting standards

In December 2007, the Financial Accounting Standards Board ("FASB") issued SFAS 160, *Noncontrolling Interests in Consolidated Financial Statements, an amendment to ARB No. 51*. This statement states that accounting and reporting for minority interests will be recharacterized as noncontrolling interests and classified as a component of equity. SFAS 160 applies to all entities that prepare consolidated financial statements, but will affect only those entities that have an outstanding noncontrolling interest in one or more subsidiaries or that deconsolidate a subsidiary. This statement is effective for fiscal years beginning after December 15, 2008. We are currently evaluating what the impact of adopting SFAS 160 will have on our results of operations and financial position.

3. Fair Value Measurements

In September 2006, the FASB issued SFAS 157, *Fair Value Measurements*. SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with accounting principles generally accepted in the United States, and expands disclosures about fair value measurements. We have adopted the provisions of SFAS 157 as of January 1, 2008. Although the adoption of SFAS 157 did not impact our financial condition, results of operations, or cash flow, we are now required to provide additional disclosures as part of our financial statements.

SFAS 157 establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include: Level 1, defined as observable inputs such as quoted prices in active markets, which includes our available-for-sale securities and equity securities in publicly-held biotechnology companies; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable, which includes our auction rate securities classified as available-for-sale securities; and Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions, which includes the derivative instruments related to the subscription right and call option granted to Abbott Molecular Inc. and the equity securities we hold in privately-held biotechnology companies.

As of March 31, 2008, we held certain assets and liabilities that are required to be measured at fair value on a recurring basis, including our available-for-sale and equity securities and our derivative instruments. The fair value of these assets and liabilities was determined using the following inputs in accordance with SFAS 157 at March 31, 2008 (in thousands):

	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Available-for-sale securities (1)	$ 326,926	$ 325,151	$ 1,775(4)	$ —
Derivative instruments (2)	3,455	—	—	3,455(5)
Equity securities (3)	5,141	3,016	—	2,125(6)
Total	$ 335,522	$ 328,167	$ 1,775	$ 5,580

(1) Included in cash and cash equivalents and short term investments on our Condensed Consolidated Balance Sheet.

(2) Included in current liabilites on our Condensed Consolidated Balance Sheet.

(3) Included in other current assets and deposits and other assets on our Condensed Consolidated Balance Sheets.

(4) Represents auction rate securities of which $1.5 million were sold in April 2008.

(5) Represents the derivative instruments related to the subscription right and call option granted to Abbott (see additional discussion in Note 5).

(6) Represents equity investments in privately-held biotechnology companies. Since the securities are not traded in active markets, we determined the fair value using the most recent financial information available.

The following table presents a reconciliation of the assets and liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) from December 31, 2007 to March 31, 2008 (in thousands):

	Derivative Instruments	Equity Securities
Balance at December 31, 2007	$ —	$ 2,125
Issuance of derivative instruments	5,376(1)	—
Adjustment to fair value included in earnings	(1,921)(2)	—
Balance at March 31, 2008	$ 3,455	$ 2,125

1) Represents the derivative instruments related to the subscription right and call option granted to Abbott (see additional discussion in Note 5).

2) The subscription right and call option granted to Abbott are revalued at the end of each reporting period and the resulting difference is included in our results of operations. For the first quarter of 2008, the adjustment to fair value resulted in a gain and is included in investment income.

Additionally, in February 2007, the FASB issued SFAS 159, *The Fair Value Option for Financial Assets and Financial Liabilities*. This statement allows entities to account for most financial instruments at fair value rather than under other applicable GAAP, such as historical cost. Under SFAS 159, an asset or liability is required to be marked to fair value every reporting period with the gain or loss from a change in fair value recorded in the statement of operations. SFAS 159 is effective for all financial statements issued for fiscal years that began after November 15, 2007.

We adopted the provisions of SFAS 159 in the first quarter of 2008. SFAS 159 permits companies to make an election to carry certain eligible financial assets and liabilities at fair value. We have made the election not to measure any additional assets and liabilities at fair value other than our available-for-sale and equity securites that are currently required by SFAS 115, *Accounting for Certain Investments in Debt and Equity Securities* and our derivative instruments that are currently required under SFAS 133, *Accounting for Derivative Instruments and Hedging Activities*, to be revalued at fair value each reporting period. Therefore, the adoption of SFAS 159 did not impact our results of operations, financial position or cash flows.

4. Long-Term Obligations

In January 2007, we completed a $162.5 million convertible debt offering, which raised proceeds of approximately $157.1 million, net of $5.4 million in issuance costs. We included the issuance costs in our balance sheet and are amortizing these costs to interest expense over the life of the debt. The $162.5 million convertible subordinated notes mature in 2027 and bear interest at $2^5/_8$%, which is payable semi-annually. The $2^5/_8$% notes are convertible, at the option of the note holders, into approximately 11.1 million shares of our common stock at a conversion price of $14.63 per share. We will be able to redeem the $2^5/_8$% notes at a redemption price equal to 100.75% of the principal amount between February 15, 2012 and February 14, 2013; 100.375% of the principal amount between February 15, 2013 and February 14, 2014; and 100% of the principal amount thereafter. Holders of the $2^5/_8$% notes also are able to require us to repurchase these notes on February 15, 2014, February 15, 2017 and February 15, 2022, and upon the occurrence of certain defined conditions, at 100% of the principal amount of the $2^5/_8$% notes being repurchased plus accrued interest and unpaid interest.

We used the net proceeds from the issuance of the 2¾% notes to repurchase our 5½% convertible subordinated notes due in 2009. In January 2007, we repurchased approximately $44.2 million aggregate principal amount of our 5½% notes at a redemption price of $44.9 million plus accrued but unpaid interest. In May 2007, we redeemed the remaining $80.8 million principal balance at a redemption price of $82.1 million plus accrued but unpaid interest. As a result of the repayment of these notes, we recognized a $3.2 million loss on the early extinguishment of debt in 2007, which included a $1.2 million non-cash write-off of unamortized debt issuance costs. Included in the first quarter 2007 Condensed Consolidated Statement of Operations was $1.2 million of the $3.2 million loss and the remainder was recorded in the second quarter of 2007.

5. Collaborative Arrangements and Licensing Agreements

The information discussed below represents partnerships we entered into during 2008. There have been no material changes to the partnerships entered into prior to 2008 from the information provided in Note 6—Collaborative Arrangements and Licensing Agreements of the Consolidated Financial Statements section, included in our Annual Report on Form 10-K for the year ended December 31, 2007.

Traditional Pharmaceutical Alliances and Licensing

Genzyme Corporation

In January 2008, we entered into a strategic alliance with Genzyme focused on the licensing of mipomersen and a research relationship. The transaction included a $175 million licensing fee, a $150 million equity investment (5 million shares of common stock at $30 per share), over $1.5 billion in milestone payments and a share of profits on mipomersen and follow-on drug(s) ranging from 30 to 50 percent of all commercial sales. The contracts are being finalized and the transaction is expected to be completed in the second quarter of 2008. Under this alliance, we will over time transition the

development responsibility to Genzyme and Genzyme will be responsible for the commercialization of mipomersen. We will participate in the funding of a portion of the development costs of mipomersen.

Genzyme has agreed that it will not sell its equity investment in Isis stock purchased in February 2008 until the earlier of four years from the date of our mipomersen license agreement, the first commercial sale of mipomersen and the termination of our mipomersen license agreement. Thereafter, Genzyme will be subject to monthly limits on the number of shares it can sell. In addition, Genzyme has agreed that until the earlier of the 10 year anniversary of the mipomersen license agreement and the date Genzyme holds less than 2% of our issued and outstanding common stock, Genzyme will not acquire any additional shares of our common stock without our consent.

The price Genzyme paid for our common stock represented a significant premium over the fair value of our common stock. Using a Black-Scholes option valuation model, we determined that the value of the premium was $100 million, which represents value Genzyme gave to us to help fund the companies' research collaboration that began in January 2008. We are amortizing this premium into revenue over the four year period of our performance beginning in the first quarter of 2008. During the first quarter of 2008, we recognized revenue of $6.3 million related to the $100 million premium, which represented 29% of our total revenue for the first quarter of 2008. Our Condensed Consolidated Balance Sheet at March 31, 2008 includes deferred revenue of $93.7 million, which represents the remaining premium.

Ibis Collaborations

Abbott Molecular Inc.

In January 2008, we, Ibis and Abbott entered into a strategic alliance master agreement pursuant to which:

- Abbott purchased Ibis common stock representing approximately 10.25% of the issued and outstanding common stock of Ibis for a total purchase price of $20 million;
- Ibis granted Abbott a subscription right to purchase an additional $20 million of Ibis common stock before July 31, 2008, which when combined with Abbott's initial investment would represent approximately 18.6% of the issued and outstanding common stock of Ibis;
- We granted Abbott a call option to acquire from us all remaining Ibis capital stock for a purchase price of $175 million, which, subject to Ibis satisfying a defined set of objectives, may be increased to as much as $190 million;
- If Abbott ultimately acquires Ibis under the call option agreement, Abbott will make the earn out payments described below, which will enable our shareholders to continue to benefit from Ibis' success.

The investment by Abbott provides Ibis the funding to take the key next steps in enhancing its value, while allowing it to remain independent and focused during the option period so as to best enable this progress. This alliance with Abbott also provides Ibis the benefit of an experienced partner in molecular diagnostics and will focus Ibis on commercial success.

If Abbott acquires from us all of the remaining Ibis capital stock under the call option, Abbott will pay us earn out payments equal to a percentage of Ibis' revenue related to sales of Ibis T5000 Biosensor Systems, including instruments, assay kits and successor products from the date of the final acquisition through December 31, 2025. These earn out payments will equal 5% of Ibis' cumulative net sales over $150 million and up to $2.1 billion, and 3% of Ibis' cumulative net sales

over $2.1 billion. The earn out payments may be reduced from 5% to as low as 2.5% and from 3% to as low as 1.5%, respectively, upon the occurrence of certain events. In addition, as part of the final acquisition, Ibis may distribute to us, immediately prior to the closing, all of Ibis' cash on hand and any receivables or other payments due to Ibis under government contracts and grants held by Ibis as of the closing.

The call option initially expires on December 31, 2008, provided that, subject to certain conditions, Abbott may extend the term of the call option through June 30, 2009. In addition, if Abbott does not exercise its subscription right by July 31, 2008, the call option will expire.

Until the expiration of the call option, we and Ibis must obtain Abbott's consent before we or Ibis can take specified actions, such as amending Ibis' certificate of incorporation, redeeming, repurchasing or paying dividends on Ibis' capital stock, issuing any Ibis capital stock, entering into a transaction for the merger, consolidation or sale of Ibis, creating any Ibis indebtedness, or entering into any Ibis strategic alliance, joint venture or joint marketing agreement. In addition, the strategic alliance contains a make whole provision such that in the event of a liquidation or change of control of Ibis, Abbott will receive a payment equal to the price paid per share of the capital stock of Ibis acquired by Abbott in the initial investment or under the subscription right, plus a yield of 3% annually from the date Abbott purchased the Ibis common stock, prior to the distribution of any proceeds to any other holders of Ibis capital stock.

Under current accounting rules, we are required to value separately each element of this transaction. We determined the value attributed to the initial stock purchase was $14.6 million and since Abbott is now a minority owner of Ibis this amount was recorded as a "Noncontrolling Interest in Ibis Biosciences, Inc." on our Condensed Consolidated Balance Sheet. As the strategic alliance progresses, this line item will be reduced by Abbott's share of Ibis' net losses, which were $105,000 in the first quarter of 2008, until the balance becomes zero. The reductions to the Noncontrolling Interest in Ibis will be reflected in our Condensed Consolidated Statement of Operations using a similar caption and will improve our reported net loss. At the close of the transaction, $5.4 million of combined value was attributed to the subscription right and call option, which is included in the current liabilities section of our Condensed Consolidated Balance Sheet. As required by current accounting rules, we revalued the subscription right and call option at March 31, 2008 resulting in a $1.9 million reduction in the liability and a corresponding gain which we included in investment income on our Condensed Consolidated Statement of Operations. We will revalue the subscription right and call option at the end of each quarter until they expire or are exercised.

6. Segment Information and Concentration of Business Risk

Segment information

We report our financial results in three reportable segments, Drug Discovery and Development, Ibis, and Regulus. Segment loss from operations includes revenue offset by research and development expenses, cost of commercial revenue for our Ibis subsidiary, selling, general and administrative expenses, and other charges attributable to the segment. See the Business Segments discussion within the "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Item 2 below for additional information on the segments.

Our Drug Discovery and Development segment generates revenue from collaborations with corporate partners and from licensing proprietary patent rights. Revenue from collaborations with corporate partners may consist of upfront payments, funding for research and development activities, milestone payments and royalties or profit sharing payments. This segment's proprietary technology to discover and characterize novel antisense inhibitors has enabled our scientists to modify the properties of our antisense drugs for optimal use with particular targets and thus, to produce a broad proprietary portfolio of drugs applicable to many disease targets.

Our Ibis subsidiary generates revenue from grants and contracts from United States government agencies, from sales of its Ibis T5000 Biosensor System and related assay kits and the analysis of samples within its assay services laboratory.

Our Regulus joint venture generates revenue from funded research programs and from collaborations with corporate partners such as the recently announced strategic alliance with GlaxoSmithKline ("GSK") in April 2008.

The following is information for revenue, loss from operations and total assets by segment (in thousands):

	Drug Discovery and Development	Ibis	Regulus	Total
Three Months Ended March 31, 2008				
Revenue:				
Research and development	$ 17,615	$ 1,784	$ 92	$ 19,491
Commercial revenue (1)	—	1,195	—	1,195
Licensing and royalty	668	—	—	668
Total segment revenue	$ 18,283	$ 2,979	$ 92	$ 21,354
Loss from operations	$ (3,499)	$ (3,897)	$ (1,435)	$ (8,831)
Total assets as of March 31, 2008	$ 366,763	$ 28,379	$ 10,282	$ 405,424
Three Months Ended March 31, 2007				
Revenue:				
Research and development	$ 426	$ 945	$ —	$ 1,371
Commercial revenue (1)	—	631	—	631
Licensing and royalty	448	—	—	448
Total segment revenue	$ 874	$ 1,576	$ —	$ 2,450
Loss from operations	$ (17,766)	$ (3,135)	$ —	$ (20,901)
Total assets as of December 31, 2007	$ 239,099	$ 9,313	$ 10,446	$ 258,858

(1) Ibis' commercial revenue has been classified as research and development revenue under collaborative agreements on our Condensed Consolidated Statements of Operations.

Concentrations of business risk

We have historically funded our operations in part from collaborations with corporate partners and as it relates to Ibis, from collaborations with various government agencies. Additionally, beginning in the second half of 2006, Ibis began selling commercial products and services. A relatively small number of partners historically have accounted for a significant percentage of our revenue. Revenue from significant partners, which is defined as 10% or more of our total revenue, was as follows:

	Three Months Ended March 31,	
	2008	2007
Partner A	38%	0%
Partner B	29%	0%
Partner C	10%	0%
Partner D	5%	37%
Partner E	4%	19%
Partner F	1%	13%

For the three months ended March 31, 2008 and 2007, we derived approximately 14% and 64%, respectively, of our revenue from agencies of the United States Government in aggregate. For the quarter ended March 31, 2008, none of our significant partners were agencies of the United States Government while two significant partners accounted for 37% and 19% of revenue from agencies of the United States Government for the quarter ended March 31, 2007.

Contract receivables from five significant partners comprised approximately 20%, 17%, 15%, 14% and 11% of contract receivables at March 31, 2008. Contract receivables from three significant partners comprised approximately 25%, 19% and 11% of contract receivables at December 31, 2007.

7. Subsequent Events

In April 2008, Regulus entered into a strategic alliance with GSK to discover, develop and market novel microRNA-targeted therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. The alliance utilizes Regulus' expertise and intellectual property position in the discovery and development of microRNA-targeted therapeutics and provides GSK with an option to license drug candidates directed at four different microRNA targets with relevance in inflammatory disease. Regulus will be responsible for the discovery and development of the microRNA antagonists through completion of clinical proof of concept, unless GSK chooses to exercise its option earlier. After exercise of the option, GSK will have an exclusive license to drugs developed under each program by Regulus for the relevant microRNA target for further development and commercialization on a worldwide basis. Regulus will have the right to further develop and commercialize any microRNA therapeutics which GSK chooses not to develop or commercialize.

Regulus received $20 million in upfront payments from GSK, including a $15 million option fee and a $5 million note. The note plus interest will convert into Regulus common stock in the future if Regulus achieves a minimum level of financing with institutional investors. In addition, we and Alnylam are guarantors of the note, and if the note does not convert or is not repaid in cash after three years, we, Alnylam and Regulus may elect to repay the note plus interest with shares of each company's common stock. Regulus could also be eligible to receive up to $144.5 million in development, regulatory and sales milestone payments for each of the four microRNA-targeted drugs discovered and developed as part of the alliance. In addition to the potential of up to nearly $600 million Regulus could receive in option, license and milestone payments, Regulus would also receive tiered royalties up to double digits on worldwide sales of drugs resulting from the alliance.

The $15 million option fee will be amortized into revenue over Regulus' six year period of performance. The $5 million note will be shown as a liability on our Condensed Consolidated Balance Sheet.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

In this Report on Form 10-Q, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us," means Isis Pharmaceuticals, Inc. and its subsidiaries.

Forward-Looking Statements

In addition to historical information contained in this Report on Form 10-Q, this Report includes forward-looking statements regarding our business, the financial position and outlook for Isis Pharmaceuticals, Inc. as well as our Ibis Biosciences subsidiary and our Regulus joint venture, and the therapeutic and commercial potential of our technologies and products in development. Any statement describing our goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' goals and projections. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, in developing and commercializing systems to identify infectious organisms that are effective and commercially attractive, and in the endeavor of building a business around such products. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning our programs are described in additional detail in our Annual Report on Form 10-K for the year ended December 31, 2007, which is on file with the U.S. Securities and Exchange Commission, and those identified within this Item entitled "Risk Factors" beginning on page 28 of this Report.

Overview

We are a leading company in antisense technology exploiting a novel drug discovery platform to create a broad pipeline of first-in-class drugs. Through our highly efficient and prolific drug discovery platform, we can expand our drug pipeline and our partner's drug pipelines with antisense drugs that address significant unmet medical needs. Our business strategy is to do what we do best–to discover unique antisense drugs and conduct early development on these drugs to key value inflection points. Because we can discover more drugs than we can develop, our plan is to discover new drugs, outlicense our drugs to partners and build a growing annuity of milestone payments and royalty income. In this way, we maximize the value of the drugs we discover by licensing our drugs to partners at key development points, which allows us to focus on utilizing our antisense technology platform to discover new drugs. At the same time, we benefit from our partner's expertise to develop, commercialize and market our drugs. For example, we partner our drugs with leading pharmaceutical companies, such as Bristol-Myers Squibb Company, Genzyme and Ortho-McNeil, Inc. as well as with smaller satellite companies that have expertise in specific disease areas. In addition to our cutting edge antisense programs, we maintain technology leadership beyond our core areas of focus through collaborations with Alnylam, Ercole Biotech, Inc. and Regulus, our joint venture created to focus on microRNA therapeutics. We explore the technology beyond antisense with additional opportunities in infectious disease identification through our Ibis subsidiary and in the discovery and development of aminoglycoside and aptamer drugs through our technology partners, Achaogen, Inc. and Archemix, respectively. All of these aspects fit into our unique business model and create continued shareholder value.

We protect our proprietary RNA-based technologies and products through our substantial and vast patent estate of more than 1,500 issued patents. We remain one of the largest patent holders in the U.S., and with our ongoing research and development, our patent portfolio continues to grow. The patents not only protect our key assets—our technology, our drugs, and the Ibis T5000 Biosensor System—they also form the basis for lucrative licensing and partnering arrangements. We have generated more than $111.5 million from our intellectual property licensing program that helps support our internal drug discovery and development programs.

In addition to the important progress we and our partners made with our second generation drugs in development and the achievements of our Ibis subsidiary in commercializing the Ibis T5000 Biosensor System, to date in 2008, we have completed several transactions that significantly strengthened our financial position. In January 2008, we entered into a strategic alliance with Genzyme and we and Ibis entered into a strategic alliance with Abbott. Additionally, in April 2008, Regulus entered into a strategic partnership with GSK. These partnerships have provided us with an aggregate of approximately $190 million in cash payments to date and the potential to earn over $2.1 billion in milestone payments. We also will share in the future commercial success of the drugs resulting from these partnerships through profit sharing and

royalties. Furthermore, in addition to the up to $210 million that we would receive if Abbott ultimately acquires Ibis, we are entitled to earn out payments based on Ibis' future cumulative sales. These transactions represent the value that we are realizing from our extensive product pipeline and the successes of our partnering strategy, and provide us with the financial strength to continue to successfully execute our goals.

As evidenced from our recent partnering successes, we continue to benefit from our business strategy that enables us to discover and develop drugs and technologies, nurturing them until the right time to progress them to partners or to satellite companies. This strategy has provided us with the financial strength and the diverse pipeline of drugs that we have today. Looking forward, we expect to grow our pipeline this year, adding two to four new drugs; already we have added the first drug with PSCK9, our development candidate with BMS for which we earned a $2 million milestone payment.

Business Segments

We focus our business on three principal segments:

Drug Discovery and Development Within our primary business segment, we are exploiting a novel drug discovery platform to create a broad pipeline of first-in-class drugs for us and our partners. Our proprietary technology enables us to rapidly identify drugs, providing a wealth of potential targets to treat a broad range of diseases. We focus our efforts in therapeutic areas where our drugs will work best, efficiently screening many targets in parallel and selecting the best drugs. The efficiency combined with our rational approach to selecting disease targets enables us to build a large and diverse portfolio of drugs designed to treat a variety of health conditions. We currently have 18 drugs in development. Our partners are licensed to develop, with our support, 15 of these 18 drugs, which substantially reduces our development costs. We focus our internal drug development programs on drugs to treat cardiovascular, metabolic and inflammatory diseases. Our partners focus on disease areas such as ocular, viral, inflammatory and neurodegenerative diseases, and cancer.

Ibis Biosciences, Inc. Ibis, formerly a wholly owned subsidiary of Isis and now a majority-owned subsidiary of Isis, has developed and is commercializing its biosensor technology, including the Ibis T5000 Biosensor System and assay kits. Ibis' T5000 offers a unique solution for rapid identification and characterization of infectious agents. It can identify virtually all bacteria, viruses and fungi and provide information about drug resistance, virulence and strain type of these pathogens within several hours. Ibis is developing, manufacturing and selling the Ibis T5000 instruments along with the Ibis T5000 assay kits. Currently we are selling research use only kits for many applications. Examples of these kits include influenza surveillance, *Staphylococcus aureus* genotyping and characterization, antibiotic resistance determination and anthrax genotyping. We continue to develop new kits, and as defined through our agreement with Abbott, we are particularly focused on developing those applications that will be of highest commercial value for the clinical diagnostics market.

Much of the development of the Ibis T5000 Biosensor System and related applications has been funded through government contracts and grants. As of March 31, 2008, we had earned $70.2 million in revenue under our government contracts and grants, and we had an additional $7.8 million committed under our existing contracts and grants.

Regulus Therapeutics LLC In September 2007, we and Alnylam established Regulus as a joint venture focused on the discovery, development, and commercialization of microRNA therapeutics. Regulus is addressing therapeutic opportunities that arise from alterations in microRNA expression. Since microRNAs regulate the expression of broad networks of genes and biological pathways, microRNA therapeutics define a new and potentially high-impact strategy to target multiple points on disease pathways.

To date, microRNAs have been implicated in several disease areas, such as cancer, viral infection, metabolic disorders, and inflammatory diseases. Regulus is currently focusing on several of these disease areas, including microRNA therapeutics that target miR-122, an endogenous liver-specific host gene also required for viral infection by hepatitis C virus, or HCV, and metabolics. Regulus is actively exploring additional areas for development of microRNA therapeutics, including cancer, other viral diseases, metabolic disorders and inflammatory diseases.

Recent Events

Mipomersen Highlights

Mipomersen, the most advanced drug in our cardiovascular pipeline, will be evaluated in a broad Phase 3 program in patients with high cholesterol at high risk for cardiovascular disease including an ongoing Phase 3 study in patients with homozygous Familial Hypercholesterolemia, or FH.

- We reported updated safety data on mipomersen from an ongoing open-label extension study in 20 patients with FH that showed that mipomersen continues to be well tolerated and maintains activity in longer-term treatment.

- We reported the results of two preclinical studies in which the lowering of ApoB-100 resulted in the dramatic reduction of atherosclerotic plaques in murine models of atherosclerosis.
- In April 2008, we received guidance from the FDA on approval requirements for mipomersen.
- We licensed mipomersen to Genzyme as part of a strategic alliance for which the contracts are being finalized and the transaction is expected to be completed this quarter. The deal included:
  - A $175 million mipomersen licensing fee
  - A $150 million equity investment (at $30 per share)
  - Over $1.5 billion in milestone payments for mipomersen
  - A share of profits on mipomersen and follow-on drug(s) ranging from 30 to 50 percent of all commercial sales.

- A preferred partner relationship for the development and commercialization of antisense drugs for CNS and certain rare diseases.

Pipeline Highlights

- We expanded our cardiovascular disease franchise with the addition of a development candidate that targets PCSK9.
  - We received a $2 million milestone payment with the selection of an antisense drug candidate to advance into development.
- OncoGenex reported encouraging Phase 2 data of OGX-011, an antisense drug in clinical studies in patients with advanced prostate or lung cancers.
- Antisense Therapeutics licensed TV-1102 (formerly ATL1102), an antisense drug in Phase 2 clinical development for patients with multiple sclerosis, to Teva Pharmaceuticals.
- Altair Therapeutics has advanced AIR 645, an antisense drug we discovered and licensed to Altair in 2007, into Phase 1 studies. AIR 645 is the first inhaled antisense drug to enter clinical development for the treatment of asthma.
- Lilly has advanced an antisense drug, LY2181308, which targets survivin for the treatment of cancer, into Phase 2 trials.

Ibis Biosciences

- Ibis, our majority-owned subsidiary, has developed and is commercializing its biosensor technology to revolutionize the way that infectious disease pathogens are identified. At the beginning of the year, Ibis completed a transaction with Abbott in which:
  - Abbott invested $20 million in Ibis and now owns 10.25 percent equity in Ibis at a post money valuation of $215 million, with the option to invest an additional $20 million in Ibis by July 31, 2008.
  - Abbott also acquired the option to purchase the remaining shares of Ibis for a total purchase price of $215 to $230 million. If Abbott exercises its option to acquire Ibis, we will receive earn out payments tied to the achievement of specific cumulative sales.
  - Ibis entered into a distribution relationship under which Abbott will be selling Ibis products.
  - Ibis was also awarded up to approximately $2.8 million in government contracts and grants.

Regulus Therapeutics

- Regulus, our joint venture formed in September 2007, is focused on developing microRNA therapeutics, as a new approach to target the pathways of human disease. In April 2008, Regulus entered into a strategic alliance with GSK that could provide up to nearly $600 million to Regulus to develop microRNA-targeted therapeutics to treat inflammatory disease.
  - Regulus received a $20 million upfront payment, including a $15 million option fee and payment for a $5 million note that will convert into Regulus common stock under certain circumstances.
  - The alliance provides GSK with an option to license drug candidates directed at four different inflammatory disease microRNA targets.
  - Regulus will receive up to $144.5 million in development, regulatory and sales milestone payments for each microRNA-targeted drug discovered and developed as part of the collaboration.
  - Regulus will also receive tiered royalties up to double digits on sales of drugs resulting from the alliance.

Critical Accounting Policies

We prepare our condensed consolidated financial statements in conformity with accounting principles generally accepted in the United States of America. As such, we are required to make certain estimates, judgments and assumptions that we believe are reasonable, based upon the information available to us. These judgments involve making estimates about the effect of matters that are inherently uncertain and may significantly impact our quarterly or annual results of operations and financial condition. Each quarter, our senior management discusses the development, selection and disclosure of such estimates with our audit committee of our Board of Directors. There are specific risks associated with these critical accounting policies and we caution that future events rarely develop exactly as expected, and that best estimates routinely require adjustment. Historically, our estimates have been accurate as we have not experienced any material differences between our estimates and our actual results. The significant accounting policies, which we believe are the most critical to aid in fully understanding and evaluating our reported financial results, require the following:

- Assessment of the propriety of revenue recognition and associated deferred revenue;
- Determination of the proper valuation of investments in marketable securities and other equity investments;
- Estimations to assess the recoverability of long-lived assets, including property and equipment, intellectual property and licensed technology;

- Determination of the proper valuation of inventory;

- Determination of the appropriate cost estimates for unbilled preclinical studies and clinical development activities;
- Estimation of our net deferred income tax asset valuation allowance;
- Determination of the appropriateness of judgments and estimates used in allocating revenue and expenses to operating segments; and
- Estimations to determine the fair value of stock-based compensation, including the expected life of the option, the expected stock price volatility over the term of the expected life and estimated forfeitures.

There have been no material changes to our critical accounting policies and estimates from the information provided in Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations", included in our Annual Report on Form 10-K for the year ended December 31, 2007.

Results of Operations

Revenue

Total revenue for the three months ended March 31, 2008 was $21.4 million compared to $2.5 million for the same period in 2007. Revenue was significantly higher in the first quarter of 2008 due to the addition of revenue from new collaborations. As part of our new strategic relationship with Genzyme, Genzyme purchased $150 million of our common stock at $30 per share. We are amortizing the premium on the stock, $100 million calculated using a Black-Scholes option valuation model, into revenue over the four year period of our performance under the collaboration beginning in the first quarter of 2008. Also contributing to the increase in our revenue was an increase in Ibis' revenue, which is discussed further in the Ibis Biosciences, Inc. section below.

Quarter-to-quarter fluctuations in revenue are common for us as our revenue is significantly affected by the nature and timing of payments under agreements with our partners, including license fees and milestone-related payments, such as the $2 million milestone payment we recently received from BMS, which will be included in revenue in the second quarter of 2008.

The following table sets forth information on our revenue by segment (in thousands):

	Three Months Ended March 31,	
	2008	2007
Drug Discovery and Development:		
Research and development revenue	$ 17,615	$ 426
Licensing and royalty revenue	668	448
	$ 18,283	$ 874
Ibis Biosciences:		
Research and development revenue	$ 1,784	$ 945
Commercial revenue (1)	1,195	631
	$ 2,979	$ 1,576
Regulus Therapeutics:		
Research and development revenue	$ 92	$ —
	$ 92	$ —
Total revenue:		
Research and development revenue	$ 19,491	$ 1,371
Commercial revenue (1)	1,195	631
Licensing and royalty revenue	668	448
	$ 21,354	$ 2,450

(1) Ibis Biosciences' commercial revenue has been classified as research and development revenue under collaborative agreements on Isis' Condensed Consolidated Statements of Operations.

Drug Discovery & Development

Research and Development Revenue Under Collaborative Agreements

Revenue for our drug discovery and development segment includes revenue from research and development under collaborative agreements and licensing and royalty revenue. Research and development revenue under collaborative agreements for the three months ended March 31, 2008 was $17.6 million, compared to $426,000 for the same period in 2007. The increase is due to revenue from our collaborations with BMS, OMI and Genzyme.

Licensing and Royalty Revenue

Our revenue from licensing activities and royalties for the three months ended March 31, 2008 was $668,000 and was slightly higher compared to $448,000 for the same period in 2007.

Ibis Biosciences, Inc.

Ibis' revenue for the first quarter ended March 31, 2008 was $3.0 million, compared to $1.6 million for the same period in 2007. As a result of the increased number of T5000 Biosensor System placements during fiscal year 2007, Ibis' commercial revenue of $1.2 million for the first quarter of 2008 was approximately double the commercial revenue of $631,000 in the first quarter of 2007. Commercial revenue consisted of revenue from sales of Ibis T5000 Biosensor Systems and assay kits, as well as revenue from Ibis' assay services business. Because Ibis provides a full year of support for each Ibis T5000 Biosensor System following installation, Ibis is amortizing the revenue for instrument and assay kits over the period of this support obligation. Ibis' revenue from government contracts was $1.8 million for the first quarter of 2008, representing an increase of 89% over $945,000 in the first quarter of 2007 driven primarily by recently awarded contracts that support commercial as well as government applications of the T5000.

From inception through March 31, 2008, Ibis has earned $70.2 million in revenue from various government agencies to further the development of our Ibis T5000 Biosensor System and related assay kits. An additional $7.8 million is committed under existing contracts and grants. Ibis may receive additional funding under these contracts based upon a variety of factors, including the accomplishment of program objectives and the exercise of contract options by the contracting agencies. These agencies may terminate these contracts and grants at their convenience at any time, even if we have fully performed our obligations. Consequently, we may never receive the full amount of the potential value of these awards.

Regulus Therapeutics

Regulus' revenue for the first quarter ended March 31, 2008 was $92,000 related to a Small Business Innovation Research grant from the National Institute of Allergy and Infectious Diseases, a part of the National Institutes of Health, which is funding further research for the miR-122 program. As part of Regulus' strategic alliance with GSK, Regulus received a $15 million option fee which will be amortized into revenue over Regulus' six year period of performance beginning in the second quarter of 2008. Because Regulus was formed in the third quarter of 2007, it did not have revenue in the first quarter of 2007.

Operating Expenses

Operating expenses for the quarter ended March 31, 2008 were $30.2 million compared to $23.4 million for the same period of 2007. We have expanded our clinical development programs, resulting in an increase in operating expenses of $1.5 million in the first quarter of 2008 compared to the first quarter of 2007. Additionally, Ibis' operating expenses have increased by $2.2 million to support the growth of its commercial business and the cost of activities to achieve milestones as part of Abbott's investment and purchase option. Also contributing to the increase in operating expenses was $1.5 million of expenses associated with our joint venture, Regulus, which are expected to increase over the year as Regulus increases its staffing and operations.

Also contributing to the increase in operating expenses was an increase in non-cash compensation expense related to stock options. Non-cash compensation expense related to stock options was $3.8 million in the first quarter of 2008 compared to $2.4 million for the same period in 2007, primarily reflecting the increase in our stock price from the first quarter of 2007 to the first quarter of 2008.

Our operating expenses by segment were as follows (in thousands):

	Three Months Ended March 31,	
	2008	2007
Drug Discovery and Development	$ 21,782	$ 18,640
Ibis Biosciences	6,876	4,711
Regulus Therapeutics	1,527	—
Total operating expenses	$ 30,185	$ 23,351

In order to analyze and compare our results of operations to other similar companies, we believe that it is important to exclude non-cash compensation expense related to stock options. We believe non-cash compensation expense is not indicative of our operating results or cash flows from our operations. Further, we internally evaluate the performance of our operations excluding it.

Research and Development Expenses

Our research and development expenses consist of costs for antisense drug discovery, antisense drug development, manufacturing and operations and R&D support costs. Also included in research and development expenses are Ibis' and Regulus' research and development expenses. The following table sets forth information on research and development costs (in thousands):

	Three Months Ended March 31,	
	2008	2007
Research and development expenses	$ 23,374	$ 18,023
Non-cash compensation expense related to stock options	3,075	1,926
Total research and development expenses	$ 26,449	$ 19,949

Our research and development expenses by segment were as follows (in thousands):

	Three Months Ended March 31,	
	2008	2007
Drug Discovery and Development	$ 19,764	$ 16,226
Ibis Biosciences	5,373	3,723
Regulus Therapeutics	1,312	—
Total research and development expenses	$ 26,449	$ 19,949

For the three months ended March 31, 2008, we incurred total research and development expenses, excluding non-cash compensation expense, of $23.4 million compared to $18.0 million for the same period in 2007. We attribute the increase to the expansion of our key programs, additional costs

required to commercialize the Ibis T5000 Biosensor System and the research efforts to support Regulus. Expenses related to Ibis and Regulus are discussed in separate sections below.

Drug Discovery & Development

Antisense Drug Discovery

Using proprietary antisense oligonucleotides to identify what a gene does, called gene functionalization, and then determining whether a specific gene is a good target for drug discovery, called target validation, are the first steps in our drug discovery process. We use our proprietary antisense technology to generate information about the function of genes and to determine the value of genes as drug discovery targets. We use this information to direct our own antisense drug discovery research, and that of our antisense drug discovery partners. Antisense drug discovery is also the function within Isis that is responsible for advancing antisense core technology.

As we continue to advance our antisense technology, we are investing in our antisense drug discovery programs to expand our and our partners' drug pipeline. We anticipate that our existing relationships and collaborations, as well as prospective new partners, will continue to help fund our research programs, as well as contribute to the advancement of the science by funding core antisense technology research.

Antisense drug discovery costs, excluding non-cash compensation expense, for the three months ended March 31, 2008 were $4.2 million compared to $3.4 million for the same period in 2007. The higher expenses in the first quarter of 2008 compared to the first quarter of 2007 were primarily due to increased activity levels related to our planned investment to fill our pipeline, initiatives aimed at reducing our costs to manufacture our drugs and additional spending to support collaborative research efforts, which required an increase in personnel and lab supplies.

Antisense Drug Development

The following table sets forth research and development expenses for our major antisense drug development projects (in thousands):

	Three Months Ended March 31,	
	2008	2007
Mipomersen	$ 3,512	$ 1,740
Other antisense development products	2,755	2,601
Development overhead costs	906	1,340
Non-cash compensation expense related to stock options	918	650
Total antisense drug development	$ 8,091	$ 6,331

Antisense drug development expenditures were $7.2 million, excluding non-cash compensation expense related to stock options, for the three months ended March 31, 2008 compared to $5.7 million for 2007. We attribute the increase primarily to the continued development of mipomersen and the initiation of the Phase 3 program for mipomersen. Development overhead costs were $906,000 for the three months ended March 31, 2008, compared to $1.3 million for the same period in 2007. The decrease in overhead costs was primarily a result of people shifting the hours they worked from non-project specific activities to specific projects related to the development of our drugs. We expect our drug development expenses to fluctuate based on the timing and size of our clinical trials.

We may conduct multiple clinical trials on a drug candidate, including multiple clinical trials for the various indications we may be studying. Furthermore, as we obtain results from trials we may elect to discontinue clinical trials for certain drug candidates in certain indications in order to focus our resources on more promising drug candidates or indications. Our Phase 1 and Phase 2 programs are research programs that fuel our Phase 3 pipeline. When our products are in Phase 1 or Phase 2 clinical trials, they are in a dynamic state where we continually adjust the development strategy for each product. Although we may characterize a product as "in Phase 1" or "in Phase 2," it does not mean that we are conducting a single, well-defined study with dedicated resources. Instead, we allocate our internal resources on a shared basis across numerous products based on each product's particular needs at that time. This means we are constantly shifting resources among products. Therefore, what we spend on each product during a particular period is usually a function of what is required to keep the products progressing in clinical development, not what products we think are most important. For example, the number of people required to start a new study is large, the number of people required to keep a study going is modest and the number of people required to finish a study is large. However, such fluctuations are not indicative of a shift in our emphasis from one product to another and cannot be used to accurately predict future costs for each product. And, because we always have numerous products in preclinical and early stage clinical research, the fluctuations in expenses from product to product, in large part, offset one another. If we partner a drug, it may affect the size of a trial, its timing, its total cost and the timing of the related cost. Our partners are developing, with our support, 15 of our 18 drug candidates, which substantially reduces our development costs. As part of our collaboration with Genzyme, we will over time transition the development responsibility to Genzyme and Genzyme will be responsible for the commercialization of mipomersen. We will participate in the funding of a portion of the development costs of mipomersen.

Manufacturing and Operations

Expenditures in our manufacturing and operations function consist primarily of personnel costs, specialized chemicals for oligonucleotide manufacturing, laboratory supplies and outside services. Manufacturing and operations expenses, excluding non-cash compensation expense, for the three months ended March 31, 2008 were $2.6 million, compared to $1.4 million for the same period in 2007. This function is responsible for providing drug supplies to antisense drug discovery and antisense drug development, including the analytical testing to satisfy good laboratory and good manufacturing practices requirements. The increase was primarily due to the costs associated with the manufacturing of drug supplies for our corporate partners and to support our expanded internal drug development programs.

R&D Support

In our research and development expenses, we include support costs such as rent, repair and maintenance for buildings and equipment, utilities, depreciation of laboratory equipment and facilities, amortization of our intellectual property, information technology costs, procurement costs and waste disposal costs. We call these costs R&D support costs.

The following table sets forth information on R&D support costs (in thousands):

	Three Months Ended March 31,	
	2008	2007
Personnel costs	$ 1,472	$ 1,281
Occupancy	1,501	1,515
Depreciation and amortization	1,120	1,205
Insurance	246	237
Other	(261)	587
Non-cash compensation expense related to stock options	641	436
Total R&D support costs	$ 4,719	$ 5,261

R&D support costs, excluding non-cash compensation expense related to stock options, for the three months ended March 31, 2008 were $4.1 million, compared to $4.8 million for the same period in 2007. The decrease was primarily a result of $750,000 we received from Ercole in March 2008 as repayment of a convertible note that we had previously expensed.

Our R&D support costs by segment were as follows (in thousands):

	Three Months Ended March 31,	
	2008	2007
Drug Discovery and Development	$ 4,010	$ 4,536
Ibis Biosciences	709	725
Total R&D support costs	$ 4,719	$ 5,261

Selling, General and Administrative Expenses

Selling, general and administrative expenses include corporate costs required to support our company, our employees and our stockholders. These costs include personnel and outside costs in the areas of business development, legal, human resources, investor relations, finance, Ibis' selling, general and administrative and Regulus' general and administrative expenses. Additionally, we include in selling, general and administrative expenses such costs as rent, repair and maintenance of buildings and equipment, depreciation, utilities, information technology and procurement costs that we need to support the corporate functions listed above. Until the acquisition of Symphony GenIsis in September 2007, selling, general and administrative expenses included Symphony GenIsis' general and administrative expenses.

The following table sets forth information on selling, general and administrative expenses (in thousands):

	Three Months Ended March 31,	
	2008	2007
Selling, general and administrative expenses	$ 3,052	$ 2,964
Non-cash compensation expense related to stock options	684	438
Total selling, general and administrative expenses	$ 3,736	$ 3,402

Our selling, general and administrative expenses by segment were as follows (in thousands):

	Three Months Ended March 31,	
	2008	2007
Drug Discovery and Development	$ 2,018	$ 2,414
Ibis Biosciences	1,503	988
Regulus Therapeutics	215	—
Total selling, general and administrative expenses	$ 3,736	$ 3,402

Selling, general and administrative expenses, excluding non-cash compensation expense related to stock options, for the three months ended March 31, 2008 were $3.1 million and were essentially flat as compared to $3.0 million for the same period in 2007. The increase in these expenses in the Ibis segment was primarily the result of additional sales and customer support costs to maintain the commercial growth of the Ibis T5000 Biosensor System. Expenses related to Ibis are discussed in a separate section below.

Ibis Biosciences, Inc.

Ibis' operating expenses include cost of goods sold for its commercial activities, research and development expenses and selling, general and administrative expenses. Ibis' research and development expenses are primarily the result of its performance under government contracts in support of the ongoing development of the Ibis T5000 Biosensor System and related assay kits. Ibis' expenses include all contract-related costs it incurs on behalf of government agencies in connection with the performance of its obligations under the respective contracts, including costs for equipment to which the government retains title. Research and development expenditures in Ibis include costs for scientists, pass-through equipment costs, laboratory supplies, chemicals and highly specialized information technology consultants to advance the research and development of the Ibis T5000 Biosensor System. Further, we allocate a portion of R&D support costs to Ibis and include this allocation in Ibis' research and development expenses. Ibis' selling, general and

administrative expenses include outside costs in the areas of business development, human resources, and finance. In addition, we allocate a portion of corporate expenses required to support Ibis to Ibis' selling, general and administrative expenses.

The following table sets forth information on Ibis' operating expenses (in thousands):

	Three Months Ended March 31,	
	2008	2007
Cost of goods sold	$ 817	$ 718
Research and development costs	3,487	1,980
R&D support costs	709	725
Selling, general and administrative expenses	1,387	879
Non-cash compensation expense related to stock options	476	409
Total Ibis' operating expenses	$ 6,876	$ 4,711

Ibis' operating expenses, excluding non-cash compensation expense related to stock options, were $6.4 million and $4.3 million for the three months ended March 31, 2008 and 2007, respectively. The increase in operating expenses primarily reflects an increase in costs to support the growth of Ibis' commercial business and the cost to achieve milestones as part of the Abbott transaction. We expect costs and expenses for Ibis to increase as we continue to expand this business.

Regulus Therapeutics

In September 2007, we and Alnylam formed Regulus, a joint venture focused on the discovery, development, and commercialization of microRNA therapeutics. Under accounting rules, we are considered the primary beneficiary of Regulus and consolidate the financial results of Regulus. As a result, our condensed consolidated financial statements include a line item called "Noncontrolling Interest in Regulus Therapeutics LLC." On our Condensed Consolidated Balance Sheet, this line reflects Alnylam's minority ownership of Regulus' equity. As the joint venture progresses, this line item will be reduced by Alnylam's share of Regulus' net losses, which were $883,000 for the first quarter of 2008

until the balance becomes zero. The reductions to the Noncontrolling Interest in Regulus will be reflected in our Condensed Consolidated Statement of Operations using a similar line item and will provide a positive adjustment to our net loss equal to Alnylam's share of Regulus' losses. With the recently announced strategic alliance with GSK, we anticipate Regulus' expenses to increase as Regulus continues to advance its research and development activities.

Investment Income

Investment income for the three months ended March 31, 2008 totaled $5.0 million compared to $3.4 million for the same period in 2007. The increase in investment income was primarily due to the $1.9 million gain resulting from the revaluation at March 31, 2008 of the the subscription right and call option granted to Abbott and a higher average cash balance in the first quarter of 2008 compared to the same period in 2007 offset by lower average returns on our investments resulting from the current market conditions. The higher average cash balance was a result of the $170 million cash payments received in the first quarter of 2008 from our strategic partnerships with Genzyme and Abbott.

Interest Expense

Interest expense for the three months ended March 31, 2008 totaled $1.4 million compared to $2.6 million for the same period in 2007. The decrease in interest expense was due to the effect of a lower debt balance in the first quarter of 2008 compared to 2007 primarily related to the fact that a portion of our old $5^1/_2$% notes was outstanding until we repaid the remaining balance in May 2007.

Gain on Investments

Gain on investments for the three months ended March 31, 2007 was $1.5 million reflecting a gain realized on the sale of a portion of the equity securities of Alnylam that we owned. We did not recognize any gain on investments for the three months ended March 31, 2008.

Loss on Early Retirement of Debt

Loss on early retirement of debt for the three months ended March 31, 2007 was $1.2 million reflecting the early extinguishment of a portion of our 5¹¤2% convertible subordinated notes in January 2007. We did not recognize any loss on early retirement of debt for the three months ended March 31, 2008.

Net Loss Applicable to Common Stock

Net loss applicable to common stock for the three months ended March 31, 2008 was $4.3 million compared to $13.0 million for the same period in 2007. Our net loss for the first quarter of 2008 was significantly lower than the first quarter of 2007 primarily due to the decrease in our loss from operations, higher investment income and lower interest expense, offset by the $6.8 million loss attributed to the noncontrolling interest in Symphony GenIsis, Inc. that we recorded in the first quarter of 2007. We did not record this benefit in the first quarter of 2008 because we purchased all of the equity of Symphony GenIsis in the third quarter of 2007, saving $75 million in the predetermined purchase price.

Net Loss Per Share

Net loss per share for the three months ended March 31, 2008 was $0.05 per share compared to $0.16 per share for the same period in 2007. The decrease in net loss per share was primarily a result of the decrease in net loss applicable to common stock discussed above.

Liquidity and Capital Resources

We have financed our operations with revenue primarily from research and development under collaborative agreements. Additionally, we have earned licensing and royalty revenue from the sale or licensing of our intellectual property. We have also financed our operations through the sale of our equity securities and the issuance of long-term debt. From our inception through March 31, 2008, we have earned approximately $598.7 million in revenue from contract research and development and the sale and licensing of our intellectual property. From the time we were founded through March 31, 2008, we have raised net proceeds of approximately $792.9 million from the sale of our equity securities and we have borrowed approximately $543.8 million under long-term debt arrangements to finance a portion of our operations.

At March 31, 2008, we had cash, cash equivalents and short-term investments of $338.4 million and stockholders' equity of $54.6 million. In comparison, we had cash, cash equivalents and short-term investments of $193.7 million and stockholders' equity of $872,000 as of December 31, 2007. As of March 31, 2008, we had consolidated working capital of $272.6 million compared to $145.1 million at December 31, 2007. The cash we received in the first quarter of 2008 from Genzyme ($150 million) and Abbott ($20 million) primarily led to the increase in our consolidated working capital offset by $25 million of deferred revenue from Genzyme that is included in current liabilities. In connection with the Genzyme transaction, we recorded the $100 million premium on the $150 million equity investment as a liability and we are amortizing it into revenue over the four year period of our performance obligation beginning in the first quarter of 2008. We recorded the remaining $50 million of proceeds as stockholders' equity.

As of March 31, 2008, our debt and other long-term obligations totaled $168.4 million, compared to $170.1 million at December 31, 2007. The decrease in our debt and other obligations was due to the declining balance on our Silicon Valley Bank term loan. We will continue to use equipment lease financing as long as the terms remain commercially attractive.

Based on our existing cash and committed cash, including the $175 million mipomersen licensing fee from Genzyme, but not including the up to $210 million we could receive from Abbott, we expect that our 2008 year end cash balance will be greater than $450 million and will last for at least five years.

The following table summarizes our contractual obligations as of March 31, 2008. The table provides a breakdown of when obligations become due. A more detailed description of the major components of our debt is provided in the paragraphs following the table:

	Payments Due by Period (in millions)				
Contractual Obligations (selected balances described below)	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**After 5 years**
$2^5/_8$% Convertible Subordinated Notes	$ 162.5	$ —	$ —	$ —	$ 162.5
Silicon Valley Bank Term Loan	$ 5.5	$ 5.5	$ —	$ —	$ —
Other Obligations	$ 0.4	$ —	$ —	$ —	$ 0.4
Operating Leases	$ 21.5	$ 3.7	$ 6.2	$ 3.0	$ 8.6

Our contractual obligations consist primarily of our publicly traded convertible debt. In addition, we also have a term loan from Silicon Valley Bank and other obligations.

In December 2003, we secured a $32.0 million term loan from Silicon Valley Bank to retire debt from two partners. We are amortizing the term loan over sixty months. The term loan requires monthly payments of principal plus accrued interest, and bears interest at the prime interest rate less applicable discounts based on the balances in the cash and investment accounts that we maintain at Silicon Valley Bank, which was 5.25% at March 31, 2008. The loan is secured by substantially all of our operating assets, excluding intellectual property, real estate, and certain equity investments. The loan is subject to certain liquidity requirements, including a requirement that we maintain a minimum balance in an account at Silicon Valley Bank at all times equal to the outstanding balance of the loan. The loan is convertible to a fixed interest rate at our option at any time at the then-applicable prime rate plus 1.25%. The carrying value of the term loan at March 31, 2008 was $5.5 million, which we expect to fully repay by December 31, 2008 according to the loan's terms.

In January 2007, we completed a $162.5 million convertible debt offering, which raised proceeds of approximately $157.1 million, net of $5.4 million in issuance costs. The $162.5 million convertible subordinated notes bear interest at $2^5/_8$%, which is payable semi-annually, and mature in 2027. The $2^5/_8$% notes are convertible, at the option of the note holders, into approximately 11.1 million shares of common stock at a conversion price of $14.63 per share. We will be able to redeem these notes at a redemption price equal to 100.75% of the principal amount between February 15, 2012 and February 14, 2013; 100.375% of the principal amount between February 15, 2013 and February 14, 2014; and 100% of the principal amount thereafter. Holders of the $2^5/_8$% notes are also able to require us to repurchase the $2^5/_8$% notes on February 15, 2014, February 15, 2017 and February 15, 2022, and upon the occurrence of certain defined conditions, at 100% of the principal amount of the $2^5/_8$% notes being repurchased plus accrued interest and unpaid interest. Using the net proceeds from the issuance of our $2^5/_8$% notes, we repaid the entire $125 million of our $5^1/_2$% convertible subordinated notes due 2009 in January and May of 2007.

In connection with the strategic alliance with GSK in April 2008, Regulus received a $5 million convertible promissory note from GSK. The convertible note bears interest at the prime rate, which was 5.25% at March 31, 2008. The note plus interest will convert into Regulus common stock in the future if Regulus achieves a minimum level of financing with institutional investors. In addition, we and Alnylam are guarantors of the note, and if the note does not convert or is not repaid in cash after three years, we, Alnylam and Regulus may elect to repay the note plus interest with shares of each company's common stock.

In addition to contractual obligations, we had outstanding purchase orders as of March 31, 2008 for the purchase of services, capital equipment and materials as part of our normal course of business.

We plan to continue to enter into collaborations with partners to provide for additional revenue to us and we may be required to incur additional cash expenditures related to our obligations under any of the new agreements we may enter into. We currently intend to use our cash and short-term equivalents to finance our activities. However, we may also pursue other financing alternatives, like issuing additional shares of our common stock, issuing debt

instruments, refinancing our existing debt, or securing lines of credit. Whether we use our existing capital resources or choose to obtain financing will depend on various factors, including the future success of our business, the prevailing interest rate environment and the condition of financial markets generally.

RISK FACTORS

Investing in our securities involves a high degree of risk. In addition to the other information in this report on Form 10-Q, you should carefully consider the risks described below before purchasing our securities. If any of the following risks actually occur, our business could be materially harmed, and our financial condition and results of operations could be materially and adversely affected. As a result, the trading price of our securities could decline, and you might lose all or part of your investment. We have marked with an asterisk those risk factors that reflect substantive changes from the risk factors included in our Annual Report on Form 10-K for the year ended December 31, 2007.

Risks Associated with our Businesses as a Whole

We have incurred losses, and our business will suffer if we fail to achieve profitability in the future.*

Because product discovery and development require substantial lead-time and money prior to commercialization, our expenses have exceeded our revenue since we were founded in January 1989. As of March 31, 2008, we had accumulated losses of approximately $832.0 million and stockholders' equity of approximately $54.6 million. Most of the losses resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. Most of our revenue has come from collaborative arrangements, with additional revenue from research grants and the sale or licensing of patents as well as interest income. We currently have only one product, Vitravene, approved for commercial use. This product has limited sales potential, and Novartis, our exclusive distribution partner for this product, no longer markets it. We expect to incur additional operating losses over the next several years, and these losses may increase if we cannot increase or sustain revenue. We may not successfully develop any additional products or services, or achieve or sustain future profitability.

Since corporate partnering is a key part of our strategy to fund the development and commercialization of our development programs, if any of our collaborative partners fail to fund our collaborative programs, or if we cannot obtain additional partners, we may have to delay or stop progress on our product development programs.

To date, corporate partnering has played a key role in our strategy to fund our development programs and to add key development resources. We plan to continue to rely on additional collaborative arrangements to develop and commercialize our products, including ISIS 113715. However, we may not be able to negotiate additional attractive collaborative arrangements.

Many of the drugs in our development pipeline are being developed and/or funded by corporate partners, including Altair Therapeutics Inc., Antisense Therapeutics Limited, Atlantic Healthcare (UK) Limited, BMS, iCo Therapeutics Inc., ImQuest Pharmaceuticals, Inc., Eli Lilly and Company, Merck & Co., Inc., OncoGenex Technologies Inc. and OMI. In addition, in January 2008 we entered a major strategic alliance with Genzyme in which Genzyme will develop and commercialize mipomersen. If any of these pharmaceutical companies stop funding and/or developing these products, our business could suffer and we may not have, or be willing to dedicate, the resources available to develop these products on our own.

Our collaborators can terminate their relationships with us under certain circumstances, some of which are outside of our control. For example, in November 2004 based on the disappointing results of the Phase 3 clinical trials, Lilly discontinued its investment in Affinitak.

In addition, the disappointing results of the two Affinitak clinical trials, our Phase 3 clinical trials of alicaforsen in patients with active Crohn's disease, or any future clinical trials could impair our ability to attract new collaborative partners. If we cannot continue to secure additional collaborative partners, our revenues could decrease and the development of our drugs could suffer.

Even with funding from corporate partners, if our partners do not effectively perform their obligations under our agreements with them, it would delay or stop the progress of our product development programs.

In addition to receiving funding, we enter into collaborative arrangements with third parties to:

- conduct clinical trials;
- seek and obtain regulatory approvals; and
- manufacture, market and sell existing and future products.

Once we have secured a collaborative arrangement to further develop and commercialize one of our development programs such as our collaborations with Genzyme, OMI and BMS, these collaborations may not continue or result in commercialized drugs, or may not progress as quickly as we anticipated.

For example, a collaborator such as Genzyme, OMI, or BMS, could determine that it is in its financial interest to:

- pursue alternative technologies or develop alternative products that may be competitive with the product that is part of the collaboration with us;
- pursue higher-priority programs or change the focus of its own development programs; or
- choose to devote fewer resources to our drugs than it does for its own drugs under development.

If any of these occur, it could affect our partner's commitment to the collaboration with us and could delay or otherwise negatively affect the commercialization of our drugs.

If we cannot protect our patents or our other proprietary rights, others may compete more effectively against us.

Our success depends to a significant degree upon our ability to continue to develop and secure intellectual property rights to proprietary products and services. However, we may not receive issued patents on any of our pending patent applications in the United States or in other countries. In addition, the scope of any of our issued patents may not be sufficiently broad to provide us with a competitive advantage. Furthermore, our issued patents or patents licensed to us may be successfully challenged, invalidated or circumvented so that our patent rights would not create an effective competitive barrier or revenue source.

In addition, our Ibis business relies in part on trade secret laws and nondisclosure, confidentiality and other agreements to protect some of the proprietary technology that is part of the Ibis T5000 Biosensor System. However, these laws and agreements may not be enforceable or may not provide meaningful protection for Ibis' trade secrets or other proprietary information in the event of unauthorized use or disclosure or other breaches of these agreements.

Until recently, virtually all of Ibis' research and development activities have been funded under contracts from the U.S. government (either directly or through subcontracts from prime contractors or higher-tier subcontractors). As a general matter, subject to certain disclosure, notice, filing, acknowledgement and reporting obligations, Ibis is entitled to retain title to any inventions conceived or first reduced to practice under government contracts, but the government will have a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced these inventions for or on behalf of the United States.

Intellectual property litigation could be expensive and prevent us from pursuing our programs.

It is possible that in the future we may have to defend our intellectual property rights. In the event of an intellectual property dispute, we may be forced to litigate to defend our rights or assert them against others. Disputes could involve arbitration, litigation or proceedings declared by the United States Patent and Trademark Office or the International Trade Commission or foreign patent authorities. Intellectual property litigation can be extremely expensive, and this expense, as well as the consequences should we not prevail, could seriously harm our business.

For example, in December 2006, the European Patent Office (EPO) Technical Board of Appeal reinstated with amended claims our Patent EP0618925 which claims a class of antisense compounds, any of which is designed to have a sequence of phosphorothioate-linked nucleotides having two regions of chemically modified RNA flanking a region of DNA. Prior to its reinstatement, this patent was originally opposed by several parties and revoked by an EPO Opposition Division in December of 2003. We intend to fully exercise our rights under this patent by pursuing licensing arrangements, but if licensing efforts are unsuccessful we may choose to assert our rights through litigation.

If a third party claims that our products or technology infringe its patents or other intellectual property rights, we may have to discontinue an important product or product line, alter our products and processes, pay license fees or cease certain activities. We may not be able to obtain a license to needed intellectual property on favorable terms, if at all. There are many patents issued or applied for in the biotechnology industry, and we may not be aware of patents or applications held by others that relate to our business. This is especially true since patent applications in the United States are filed confidentially. Moreover, the validity and breadth of biotechnology patents involve complex legal and factual questions for which important legal issues remain unresolved.

If we fail to obtain timely funding, we may need to curtail or abandon some of our programs.

All of our drugs are undergoing clinical trials or are in the early stages of research and development. All of our drugs under development will require significant additional research, development, preclinical and/or clinical testing, regulatory approval and a commitment of significant additional resources prior to their commercialization. Based on our existing cash and committed cash, including the $175 million mipomersen licensing fee from Genzyme, but not including the up to $210 million we could receive from Abbott, we expect that our 2008 year end cash balance will be greater than $450 million and will last for at least five years. If we do not meet our goals to commercialize our products, or to license our drugs and proprietary technologies, we will need additional funding in the future. Our future capital requirements will depend on many factors, such as the following:

- changes in existing collaborative relationships and our ability to establish and maintain additional collaborative arrangements;
- continued scientific progress in our research, drug discovery and development programs;
- the size of our programs and progress with preclinical and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- competing technological and market developments, including the introduction by others of new therapies that address our markets;
- success in developing and commercializing a business based on our Ibis T5000 Biosensor System to identify infectious organisms; and
- the profile and launch timing of our drugs.

If we need additional funds, we may need to raise them through public or private financing. Additional financing may not be available at all or on acceptable terms. If we raise additional funds by issuing equity securities, the shares of existing stockholders will be diluted and their price, as well as the price of our other securities, may decline. If adequate funds are not available or not available on acceptable terms, we may have to cut back on one or more of our research, drug discovery or development programs. For example, in January 2005 we decided to terminate the development of two lower priority drugs, ISIS 14803 and ISIS 104838. Alternatively, we may obtain funds through arrangements with collaborative partners or others, which could require us to give up rights to certain of our technologies, drugs or products.

If we do not progress in our programs as anticipated, the price of our securities could decrease.*

For planning purposes, we estimate and may disclose the timing of a variety of clinical, regulatory and other milestones, such as when we anticipate a certain drug will enter the clinic, when we anticipate completing a clinical trial, or when we anticipate filing an application for marketing approval. We base our estimates on present facts and a variety of assumptions. Many underlying assumptions are outside of our control. If we do not achieve milestones in accordance with our or investors' expectations, the price of our securities would likely decrease.

For example, in April 2008 the FDA provided guidance regarding approval requirements for mipomersen. The FDA indicated that reduction of LDL-cholesterol is an acceptable surrogate endpoint for accelerated approval of mipomersen for use in patients with homozygous familial hypercholesterolemia, or hoFH. The FDA will require data from two ongoing preclinical studies for carcinogenicity to be included in the hoFH filing, which is now anticipated to take place in 2010. The FDA also indicated that for broader indications in high risk, high cholesterol patients an outcome study would be required for approval. This FDA guidance caused us to revise our development plans and timelines to accelerate our planned outcome trial.

The loss of key personnel, or the inability to attract and retain highly skilled personnel, could make it more difficult to run our business and reduce our likelihood of success.

We are dependent on the principal members of our management and scientific staff. We do not have employment agreements with any of our executive officers that would prevent them from leaving us. The loss of our management and key scientific employees might slow the achievement of important research and development goals. It is also critical to our success that we recruit and retain qualified scientific personnel to perform research and development work. We may not be able to attract and retain skilled and experienced scientific personnel on acceptable terms because of intense competition for experienced scientists among many pharmaceutical and health care companies, universities and non-profit research institutions. In addition, failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

If the price of our securities continues to be highly volatile, this could make it harder for you to liquidate your investment and could increase your risk of suffering a loss.

The market price of our common stock, like that of the securities of many other biopharmaceutical companies, has been and is likely to continue to be highly volatile. These fluctuations in our common stock price may significantly affect the trading price of our securities. During the 12 months preceding March 31, 2008, the market price of our common stock ranged from $8.79 to $20.15 per share. Many factors can affect the market price of our securities, including, for example, fluctuations in our operating results, announcements of collaborations, clinical trial results, technological innovations or new products being developed by us or our competitors, governmental regulation, regulatory approval, developments in patent or other proprietary rights, public concern regarding the safety of our drugs and general market conditions.

Because we use biological materials, hazardous materials, chemicals and radioactive compounds, if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research, development and manufacturing activities involve the use of potentially harmful biological materials as well as materials, chemicals and various radioactive compounds that could be hazardous to human health and safety or the environment. These materials and various wastes resulting from their use are stored at our facilities in Carlsbad, California pending ultimate use and disposal. We cannot completely eliminate the risk of contamination, which could cause:

- interruption of our research, development and manufacturing efforts;
- injury to our employees and others;
- environmental damage resulting in costly clean up; and
- liabilities under federal, state and local laws and regulations governing health and human safety, as well as the use, storage, handling and disposal of these materials and resultant waste products.

In such an event, we may be held liable for any resulting damages, and any such liability could exceed our resources. Although we carry insurance in amounts and type that we consider commercially reasonable, we do not have insurance coverage for losses relating to an interruption of our research, development or manufacturing efforts caused by contamination, and we cannot be certain that the coverage or coverage limits of our insurance policies will be adequate. In the event our losses exceed our insurance coverage, our financial condition would be adversely affected.

If a natural or man-made disaster strikes our research and development facilities, it could delay our progress developing and commercializing our drugs or our Ibis T5000 Biosensor System.

We are developing our Ibis T5000 Biosensor System in our facility located in Carlsbad, California. Additionally, we manufacture our research and clinical supplies in a separate manufacturing facility located in Carlsbad, California. The facilities and the equipment we use to develop the Ibis T5000 Biosensor System and manufacture our drugs would be costly to replace and could require substantial lead time to repair or replace. Either of our facilities may be harmed by natural or man-made disasters, including, without limitation, earthquakes, floods, fires and acts of terrorism, and in the event they are affected by a disaster, our development and commercialization efforts would be delayed. Although we possess insurance for damage to our property and the disruption of our business from casualties, this insurance may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, or at all.

Provisions in our certificate of incorporation, other agreements and Delaware law may prevent stockholders from receiving a premium for their shares.

Our certificate of incorporation provides for classified terms for the members of our board of directors. Our certificate also includes a provision that requires at least 66% of our voting stockholders to approve a merger or certain other business transactions with, or proposed by, any holder of 15% or more of our voting stock, except in cases where certain directors approve the transaction or certain minimum price criteria and other procedural requirements are met.

Our certificate of incorporation also requires that any action required or permitted to be taken by our stockholders must be taken at a duly called annual or special meeting of stockholders and may not be taken by written consent. In addition, only our board of directors, chairman of the board or chief executive officer can call special meetings of our stockholders. We also have implemented a stockholders' rights plan, also called a poison pill, which could make it uneconomical for a third party to acquire our company on a hostile basis. These provisions, as well as Delaware law and other of our agreements, may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices, and may limit the ability of our stockholders to approve transactions that they think may be in their best interests. In addition, our board of directors has the authority to fix the rights and preferences of and issue shares of preferred stock, which may have the effect of delaying or preventing a change in control of our company without action by our stockholders.

In addition, the provisions of our convertible subordinated notes could make it more difficult or more expensive for a third party to acquire us. Upon the occurrence of certain transactions constituting a fundamental change, holders of the notes will have the right, at their option, to require us to repurchase all of their notes or a portion of their notes, which may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over the then current market prices.

Future sales of our common stock in the public market could adversely affect the trading price of our securities.

Future sales of substantial amounts of our common stock in the public market, or the perception that such sales could occur, could adversely affect trading prices of our securities. For example, we registered for resale 12,000,000 shares of our common stock and 2,999,998 shares of our common stock issuable upon the exercise of the warrants we issued as part of our August 2005 private placement as well as 4.25 million shares of our common stock issuable upon the exercise of the warrant we issued to Symphony GenIsis Holdings. In addition, on December 22, 2005, we filed a Form S-3 shelf registration statement with the SEC to register up to $200,000,000 worth of our common stock for possible issuance. Finally, we have registered for resale our $2^5/_8\%$ convertible subordinated notes, including the approximately 11,111,116 shares issuable upon conversion of the notes. The addition of any of these shares into the public market may have an adverse effect on the price of our securities.

Our business is subject to changing regulations for corporate governance and public disclosure that has increased both our costs and the risk of noncompliance.

Each year we are required to evaluate our internal controls systems in order to allow management to report on and our Independent Registered Public Accounting Firm to attest to, our internal controls as required by Section 404 of the Sarbanes-Oxley Act. As a result, we will incur additional expenses and will suffer a diversion of management's time. In addition, if we cannot continue to comply with the requirements of Section 404 in a timely manner, we might be subject to sanctions or investigation by regulatory authorities, such as the SEC, the Public Company Accounting Oversight Board (PCAOB) or the Nasdaq Global Market. Any such action could adversely affect our financial results and the market price of our common stock.

The accounting method for our convertible debt securities may be subject to change.

A convertible debt security providing for share and/or cash settlement of the conversion value and meeting specified requirements under EITF Issue No. 00-19, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*, including our outstanding convertible debt securities, is currently classified in its entirety as debt. No portion of the carrying value of such a security related to the conversion option indexed to the issuer's stock is classified as equity. In addition, interest expense is recognized at the stated coupon rate. The coupon rate of interest for convertible debt securities, including our convertible debt securities, is typically lower than what an issuer would be required to pay for nonconvertible debt with otherwise similar terms.

The EITF recently considered whether the accounting for convertible debt securities that requires or permits settlement in cash either in whole or in part upon conversion, "cash settled convertible debt securities," should be changed, but was unable to reach a consensus and discontinued deliberations on this issue. Subsequently, in July 2007, the FASB voted unanimously to reconsider the current accounting for cash settled convertible debt securities, which includes our outstanding convertible debt securities. In August 2007, the FASB exposed for public comment a proposed FASB Staff Position ("FSP") that would change the method of accounting for such securities and would require the proposed method to be retrospectively applied. The FSP, if issued as proposed, would become effective for calendar year end companies like us in the first quarter of 2009. Under this proposed method of accounting, the debt and equity components of our convertible debt securities would be bifurcated and accounted for separately in a manner that would result in recognizing interest on these securities at effective rates more comparable to what we would have incurred had we issued nonconvertible debt with otherwise similar terms. The equity component of our convertible debt securities would be included in the paid-in-capital section of stockholders' equity on our balance sheet and, accordingly, the initial carrying values of these debt securities would be reduced. Our net income for financial reporting purposes would be reduced by recognizing the accretion of the reduced carrying values of our convertible debt securities to their face amounts as additional non-cash interest expense. Therefore, if the proposed method of accounting for cash settled convertible debt securities is adopted by the FASB as described above, it would have an adverse impact on our past and future reported financial results.

We cannot predict the outcome of the proposed FSP. We also cannot predict any other changes in GAAP that may be made affecting accounting for convertible debt securities, some of which could have an adverse impact on our past or future reported financial results.

Risks Associated with our Drug Discovery and Development Business

If we or our partners fail to obtain regulatory approval for our drugs, we will not be able to sell them.

We and our partners must conduct time-consuming, extensive and costly clinical trials to show the safety and efficacy of each of our drugs, including mipomersen and ISIS 113715, before a drug can be approved for sale. We must conduct these trials in compliance with FDA regulations and with comparable regulations in other countries. If the FDA or another regulatory agency believes that we or our partners have not sufficiently demonstrated the safety or efficacy of our drugs, including mipomersen and ISIS 113715, it will not approve them or will require additional studies, which can be time consuming and expensive and which will delay commercialization of a drug. We and our partners may not be able to obtain necessary regulatory approvals on a timely basis, if at all, for any of our drugs, including mipomersen and ISIS 113715. Failure to receive these approvals or delays in these approvals could prevent or delay commercial introduction of a product, including mipomersen and ISIS 113715, and, as a result, could negatively impact our ability to generate revenue from product sales. In addition, following approval of a drug, we and our partners must comply with comprehensive government regulations regarding how we

manufacture, market and distribute drug products. If we fail to comply with these regulations, regulators could force us to withdraw a drug from the market or impose other penalties or requirements that also could have a negative impact on our financial results.

We have only introduced one commercial drug product, Vitravene. We cannot guarantee that any of our other drugs, including mipomersen and ISIS 113715, will be safe and effective, will be approved for commercialization or that our partners or we can successfully commercialize these drugs.

If the results of clinical testing indicate that any of our drugs under development are not suitable for commercial use we may need to abandon one or more of our drug development programs.

Drug discovery and development has inherent risks and the historical failure rate for drugs is high. Antisense technology in particular is relatively new and unproven. If we cannot demonstrate that our drugs, including mipomersen and ISIS 113715, are safe and effective drugs for human use, we may need to abandon one or more of our drug development programs.

In the past, we have invested in clinical studies of drugs that have not met the primary clinical end points in their Phase 3 studies. In March 2003, we reported the results of a Phase 3 clinical trial of Affinitak in patients with late-stage non-small cell lung cancer and in October 2004, we reported the results of a second similar Phase 3 clinical trial. In each case, Affinitak failed to demonstrate improved survival sufficient to support an NDA filing. In December 2004, we reported the results of our Phase 3 clinical trials of alicaforsen in patients with active Crohn's disease, in which alicaforsen did not demonstrate statistically significant induction of clinical remissions compared to placebo. Similar results could occur with the clinical trials for our other drugs, including mipomersen and ISIS 113715. If any of our drugs in clinical studies, including mipomersen and ISIS 113715, do not show sufficient efficacy in patients with the targeted indication, it could negatively impact our development and commercialization goals for these and other drugs and our stock price could decline.

Even if our drugs are successful in preclinical and early human clinical studies, these results do not guarantee the drugs will be successful in late-stage clinical trials.

Successful results in preclinical or early human clinical trials, including the Phase 2 results for mipomersen and ISIS 113715, may not predict the results of late-stage clinical trials. There are a number of factors that could cause a clinical trial to fail or be delayed, including:

- the clinical trial may produce negative or inconclusive results;
- regulators may require that we hold, suspend or terminate clinical research for noncompliance with regulatory requirements;
- we, our partners, the FDA or foreign regulatory authorities could suspend or terminate a clinical trial due to adverse side effects of a drug on subjects or patients in the trial;
- we may decide, or regulators may require us, to conduct additional preclinical testing or clinical trials;
- enrollment in our clinical trials may be slower than we anticipate;
- the cost of our clinical trials may be greater than we anticipate; and
- the supply or quality of our drugs or other materials necessary to conduct our clinical trials may be insufficient, inadequate or delayed.

Any failure or delay in one of our clinical trials, including our Phase 2 or Phase 3 development programs for mipomersen and ISIS 113715, could reduce the commercial viability of our drugs, including mipomersen and ISIS 113715.

If the market does not accept our products, we are not likely to generate revenues or become profitable.

Our success will depend upon the medical community, patients and third-party payors accepting our products as medically useful, cost-effective and safe. We cannot guarantee that, if approved for commercialization, doctors will use our products to treat patients. We currently have one commercially approved drug product, Vitravene, a treatment for cytomegalovirus, or CMV, retinitis in AIDS patients, which addresses a small market. Our partners and we may not successfully commercialize additional products.

The degree of market acceptance for any of our products depends upon a number of factors, including:

- the receipt and scope of regulatory approvals;
- the establishment and demonstration in the medical and patient community of the efficacy and safety of our drugs and their potential advantages over competing products;
- the cost and effectiveness of our drugs compared to other available therapies;
- the patient convenience of the dosing regimen for our drugs; and
- reimbursement policies of government and third-party payors.

Based on the profile of our drugs, physicians, patients, patient advocates, payors or the medical community in general may not accept and use any products that we may develop.

If we cannot manufacture our drug products or contract with a third party to manufacture our drug products at costs that allow us to charge competitive prices to buyers, we will not be able to market products profitably.

If we successfully commercialize any of our drugs, we would be required to establish large-scale commercial manufacturing capabilities either on our own or through a third party manufacturer. In addition, as our drug development pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. We have limited experience manufacturing pharmaceutical products of the chemical class represented by our drugs, called oligonucleotides, on a commercial scale for the systemic administration of a drug. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our drugs, and some of these suppliers will need to increase their scale of production to meet our projected needs for commercial manufacturing. Further, we must continue to improve our manufacturing processes to allow us to reduce our product costs. We may not be able to manufacture at a cost or in quantities necessary to make commercially successful products.

Also, manufacturers, including us, must adhere to the FDA's current Good Manufacturing Practices regulations, which the FDA enforces through its facilities inspection program. We and our contract manufacturers may not be able to comply or maintain compliance with Good Manufacturing Practices regulations. Non-compliance could significantly delay or prevent our receipt of marketing approval for potential products or result in FDA enforcement action after approval that could limit the commercial success of our potential products.

If our drug discovery and development business fails to compete effectively, our drugs will not contribute significant revenues.

Our competitors are engaged in all areas of drug discovery throughout the world, are numerous, and include, among others, major pharmaceutical companies and specialized biopharmaceutical firms. Other companies are engaged in developing antisense technology. Our competitors may succeed in developing drugs that are:

- priced lower than our drugs;
- safer than our drugs; or
- more effective than our drugs.

These competitive developments could make our products obsolete or non-competitive.

Certain of our partners are pursuing other technologies or developing other drugs either on their own or in collaboration with others, including our competitors, to develop treatments for the same diseases targeted by our own collaborative programs. Competition may negatively impact a partner's focus on and commitment to our drugs and, as a result, could delay or otherwise negatively affect the commercialization of our drugs.

Many of our competitors have substantially greater financial, technical and human resources than we do. In addition, many of these competitors have significantly greater experience than we do in conducting preclinical testing and human clinical trials of new pharmaceutical products and in obtaining FDA and other regulatory approvals of products for use in health care. Accordingly, our competitors may succeed in obtaining regulatory approval for products earlier than we do. We will also compete with respect to marketing and sales capabilities, areas in which we have limited or no experience.

Disagreements between Alnylam and us regarding the development of our microRNA technology may cause significant delays and other impediments in the development of this technology, which could negatively affect the value of the technology and our investment in Regulus.

Regulus is our joint venture with Alnylam focused on the discovery, development, and commercialization of microRNA. As part of this joint venture, we exclusively licensed to Regulus our intellectual property rights covering microRNA. Regulus is operated as an independent company and governed by a managing board comprised of an equal number of directors appointed by each of Alnylam and us. Regulus researches and develops microRNA projects and programs pursuant to an operating plan that is approved by the managing board. Any disagreements between Alnylam and us regarding a development decision or any other decision submitted to Regulus' managing board may cause significant delays in the development and commercialization of our microRNA technology and could negatively affect the value of our investment in Regulus.

We depend on third parties in the conduct of our clinical trials for our drugs and any failure of those parties to fulfill their obligations could adversely affect our development and commercialization plans.

We depend on independent clinical investigators, contract research organizations and other third-party service providers in the conduct of our clinical trials for our drugs and expect to continue to do so in the future. For example, Medpace is the primary clinical research organization for clinical trials for mipomersen. We rely heavily on these parties for successful execution of our clinical trials, but do not control many aspects of their activities. For example, the investigators are not our employees. However, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Third parties may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or our stated protocols. The failure of these third parties to carry out their obligations or a termination of our relationship with these third parties could delay or prevent the development, approval and commercialization of our drugs, including mipomersen.

Risks Associated With Our Ibis Biosciences Business

We may not successfully develop or derive revenues from our business based on our Ibis T5000 Biosensor System.

Our Ibis T5000 Biosensor System is subject to the risks inherent in developing tools based on innovative technologies. Our product is at an early stage of development and requires continued research and development to achieve our business objectives. For Ibis to be commercially successful, we must convince potential customers that our Ibis T5000 Biosensor System is an attractive alternative to existing methods of identifying pathogens. If our potential customers fail to purchase our Ibis T5000 Biosensor System due to competition or other factors, or if we fail to develop applications that lead to market acceptance, we may not recover our investment in this technology and our Ibis T5000 Biosensor System business could fail to meet our business and financial objectives.

If we fail to sell the Ibis T5000 Biosensor System to a minimum customer base, our ability to generate revenues from sales of assay kits will be negatively affected.

A key element of our business plan for Ibis calls for us to deploy the Ibis T5000 Biosensor System to a broad customer base. If we cannot create a broad installed base of our Ibis T5000 Biosensor System, our ability to sell assay kits, the consumables used to operate the system, may be significantly and adversely affected. Even if we successfully achieve broad installation of the Ibis T5000 Biosensor System, customers may not perform as many analyses as we anticipate, which may affect the assumptions underlying our business plan for Ibis and lead to lower-than-expected revenues.

We will depend on Bruker Daltonics to manufacture the Ibis T5000 Biosensor System and any failure of Bruker Daltonics to fulfill its obligations could harm or delay our commercialization efforts.

In July 2006, we entered into a strategic alliance with Bruker Daltonics to manufacture and distribute the Ibis T5000 Biosensor System. Bruker Daltonics will be the exclusive, worldwide manufacturer of the Ibis T5000 Biosensor System and will also be responsible for order processing, system installations and service in North America, Europe and the Middle East. In Europe and the Middle East, Bruker Daltonics will have exclusive rights to sell Ibis T5000 Biosensor Systems and Ibis assay kits for various government applications, and non-exclusive rights to sell to customers for all other applications except diagnostics. As such, we rely heavily on Bruker Daltonics to successfully manufacture, distribute and service our Ibis T5000 Biosensor System, but do not control many aspects of Bruker Daltonics activities. We believe Bruker Daltonics has failed to satisfactorily perform its obligations under the agreement. We have initiated the formal dispute resolution process under the agreement so that we can improve the manufacture, service and sales of our Ibis T5000 Biosensor Systems. If Bruker Daltonics continues to fail to carry out its obligations under our alliance, its failure could harm or delay the commercialization of our Ibis T5000 Biosensor System.

Ibis' strategic alliance with Abbott may restrict the way Ibis conducts its business and may not result in the ultimate sale of Ibis to Abbott.

On January 30, 2008, we and Ibis entered into a Strategic Alliance Master Agreement with Abbott. As part of this transaction, we granted Abbott an exclusive option to acquire from us all remaining Ibis capital stock. Under the exclusive option, we and Ibis must obtain Abbott's consent before we or Ibis can take specified actions, such as amending Ibis' certificate of incorporation, redeeming, repurchasing or paying dividends on Ibis capital stock, issuing any Ibis capital stock, entering into a transaction for the merger, consolidation or sale of Ibis, creating any Ibis indebtedness, or entering into any Ibis strategic alliance, joint venture or joint marketing agreement. These consent requirements may restrict the way Ibis conducts its business and may discourage others from trying to collaborate with or buy our Ibis subsidiary. Abbott's decision to exercise the exclusive option is at its sole discretion. As a result, we cannot guarantee that Abbott will exercise its option to acquire the remaining Ibis capital stock. If Abbott does not exercise its option to acquire the remaining Ibis capital stock, we will not realize the full benefit of the strategic alliance and we may need to secure a new partner to further expand the Ibis business into the areas of hospital associated infection control and infectious disease diagnostics.

We depend on government contracts for most of Ibis' revenues and the loss of government contracts or a decline in funding of existing or future government contracts could adversely affect our revenues and cash flows.

Historically, most of Ibis' revenues were from the sale of services and products to the U.S. government. The U.S. government may cancel these contracts at any time without penalty or may change its requirements, programs or contract budget or decline to exercise option periods, even if we have fully performed our obligations. Since a large portion of Ibis' government contracts are milestone based, if Ibis fails to meet a specific milestone within the specified delivery date, our government partner may be more likely to reduce or cancel its contract with Ibis. Our revenues and cash flows from U.S. government contracts could also be reduced by declines in U.S. defense, homeland security and other federal agency budgets.

For the three months ended March 31, 2008 and 2007, we derived approximately 14% and 64%, respectively, of our revenue from agencies of the U.S. government. Because of the concentration of our contracts, we are vulnerable to adverse changes in our revenues and cash flows if a significant number of our U.S. government contracts and subcontracts are simultaneously delayed or canceled for budgetary, performance or other reasons.

If U.S. defense and other federal agencies choose to reduce their purchases under our contracts, exercise their right to terminate contracts, fail to exercise options to renew contracts or limit our ability to obtain new contract awards, our revenues and cash flows could be adversely affected.

We may be liable for penalties under a variety of procurement rules and regulations, and changes in government regulations could adversely impact our revenues, operating expenses and operating margins.

Under our agreements with the U.S. government, we must comply with and are affected by various government regulations that impact our operating costs, operating margins and our internal organization and operation of our businesses. These regulations affect how our customers and we do business and, in some instances, impose added costs on our businesses. Any changes in applicable laws could adversely affect the financial performance of Ibis. With respect to U.S. government contracts, any failure to comply with applicable laws could result in contract termination, price or fee reductions or suspension or debarment from contracting with the U.S. government. Among the most significant regulations are the following:

- the U.S. Federal Acquisition Regulations, which comprehensively regulate the formation, administration and performance of government contracts;

- the U.S. Truth in Negotiations Act, which requires certification and disclosure of all cost and pricing data in connection with contract negotiations; and

- the U.S. Cost Accounting Standards, which impose accounting requirements that govern our right to reimbursement under certain cost-based government contracts.

If our Ibis T5000 Biosensor System's reliability does not meet market expectations, we may be unable to retain our existing customers and attract new customers.

Complex instruments such as our Ibis T5000 Biosensor System typically require operating and reliability improvements following their initial introduction. As we continue to develop our Ibis T5000 Biosensor System and its related applications, we will need to make sure our customers are satisfied with the sensor's reliability. Our efforts to satisfy our customer's needs for instrument reliability could result in greater than anticipated service expenses or divert other resources. Additionally, if we fail to resolve reliability issues as they develop, we could materially damage our reputation, which could prevent us from retaining our existing customers and attracting new customers.

If we had to replace a supplier of one of the major hardware components of our Ibis T5000 Biosensor System, it could delay our commercialization efforts and lengthen our sales cycle.

We have a single supplier for each major hardware component of our Ibis T5000 Biosensor System. Although, we believe we would be able to find a replacement provider, if any of these suppliers stopped providing us with their respective components, identifying and securing a suitable replacement could delay our commercialization efforts and lengthen our sales cycle. For example, Bruker Daltonics supplies the mass spectrometer we use as part of our Ibis T5000 Biosensor System.

If Ibis fails to compete effectively, it may not succeed or contribute significant revenues.

The market for products such as Ibis' is highly competitive. Currently, large reference laboratories, public health laboratories and hospitals perform the majority of diagnostic tests used by physicians and other health care providers. We expect that these laboratories will compete vigorously to maintain their dominance in the diagnostic testing market. To remain competitive, we will need to continually improve Ibis' products so that, when compared to alternatives, its products:

- provide faster results;
- are cost-effective;
- deliver more accurate information;
- are more user friendly; and
- support a broad range of applications.

If Ibis cannot keep its products ahead of its competitors in these areas, Ibis' revenues will suffer and we may not meet our commercialization goals.

Many of Ibis' competitors have, and in the future these and other competitors may have, significantly greater financial, marketing, sales, manufacturing, distribution and technological resources than Ibis. Moreover, these companies may have substantially greater expertise in conducting clinical trials and research and development, greater ability to obtain necessary intellectual property licenses and greater brand recognition than Ibis. In addition, Ibis' competitors may be in a better position to respond quickly to new or emerging technologies, may be able to undertake more extensive marketing campaigns, may adopt more aggressive pricing policies and may be more successful in attracting potential customers, employees and strategic partners than Ibis.

Improvements in preventing major diseases could reduce the need for our Ibis T5000 Biosensor System and related assay kits, which in turn could reduce our revenues.

We expect to derive a significant portion of our Ibis revenues from the sale of assay kits necessary to use our Ibis T5000 Biosensor System. The need to quickly identify and contain major threats, such as the avian flu, could increase the demand for our assay kits. Conversely, improvements in containing or treating a threat, such as vaccines, would significantly reduce the need to identify and contain the threat. Any reduction in the need to identify or contain a threat could diminish the need for our assay kits, which could reduce our revenues.

Our plans to commercialize the Ibis T5000 Biosensor System internationally are subject to additional risks that could negatively affect our operating results.

Our success will depend in part on our ability and Bruker Daltonics' ability to market and sell the Ibis T5000 Biosensor System and assay kits in foreign markets. Expanding our international operations could impose substantial burdens on our resources, divert management's attention from domestic operations and otherwise adversely affect our business. Furthermore, international operations are subject to several inherent risks including:

- trade protective measures and import or export licensing requirements or other restrictive actions by U.S. and foreign governments could prevent or limit our international sales;
- reduced protection of intellectual property rights;
- changes in foreign currency exchange rates;
- changes in specific country's or region's political or economic conditions; and
- changes in tax laws.

If we cannot access or license rights to particular nucleic acid sequences for targeted diseases in the future, we may be limited in our ability to develop new products and access new markets.

Although our research staff seeks to discover particular nucleic acid sequences for targeted diseases, our ability to offer diagnostic tests for diseases may depend on the ability of third parties to discover particular sequences or markers and correlate them with disease, as well as the rate at which such discoveries are made. Our ability to design products that target these diseases may depend on our ability to obtain the necessary access to raw materials or intellectual property rights from third parties who make any of these discoveries. If we are unable to access new technologies or the rights to particular sequences or markers necessary for additional diagnostic products on commercially reasonable terms or at all, we may not be able to develop new diagnostic products or enter new markets.

The sales cycles for our Ibis T5000 Biosensor Systems are lengthy, and we may expend substantial funds and management effort with no assurance of successfully selling our Ibis T5000 Biosensor Systems or services.

The sales cycles for Ibis T5000 Biosensor Systems are typically lengthy. Our sales and licensing efforts, and those of our partners, will require the effective demonstration of the benefits, value, and differentiation and validation of our products and services, and significant training of multiple personnel and departments within a potential customer organization. We or our partners may be required to negotiate agreements containing terms unique to each prospective customer or licensee, which would lengthen the sales cycle. We may expend substantial funds and management effort with no assurance that we will sell our products. In addition, this lengthy sales cycle makes it more difficult for us to accurately forecast revenue in future periods and may cause revenues and operating results to vary significantly in future periods.

If we or our partners are required to obtain regulatory approval for our Ibis T5000 Biosensor System, we may not successfully obtain approval.

Ibis' business plan assumes a significant portion of its revenues will come from Ibis T5000 Biosensor Systems and assay kits for *in vitro* diagnostic purposes, whose uses are regulated by the FDA and comparable agencies of other countries. In addition, customers may wish to utilize the Ibis T5000 Biosensor System and assay kits in manners that require additional regulatory approval. To access these markets, Ibis' products may require either premarket approval or 510(k) clearance from the FDA and other regulatory agencies prior to marketing. The 510(k) clearance process usually takes from three to twelve months from submission, but can take longer. The premarket approval process is much more costly, lengthy, and uncertain and generally takes from six months to two years or longer from submission. In addition, commercialization of any

diagnostic or other product that our licensees or collaborators or we develop would depend upon successful completion of preclinical testing and clinical trials. Preclinical testing and clinical trials are long, expensive and uncertain processes, and we do not know whether we, our licensees or any of our collaborators, would be permitted or able to undertake clinical trials of any potential products. It may take us or our licensees or collaborators many years to complete any such testing, and failure could occur at any stage. Preliminary results of clinical trials do not necessarily predict final results, and acceptable results in early clinical trials may not be repeated in later clinical trials. We or our collaborators may encounter delays or rejections of potential products based on changes in regulatory policy for product approval during the period of product development and regulatory agency review. If our Ibis T5000 Biosensor System is considered a medical device, after gaining market approval from the FDA, our Ibis T5000 Biosensor System may be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, recordkeeping and reporting of safety and other post-market information.

If we become subject to product liability claims relating to Ibis, we may be required to pay damages that exceed our insurance coverage.

Any product liability claim brought against us with respect to Ibis, with or without merit, could result in the increase of our product liability insurance rates or the inability to secure coverage in the future. Expenses incurred by our insurance provider in defending these claims will reduce funds available to settle claims or pay adverse judgments. In addition, we could be liable for amounts in excess of policy limits, which would have to be paid out of our cash reserves, and our cash reserves may be insufficient to satisfy the liability. Finally, even a meritless or unsuccessful product liability claim could harm Ibis' reputation in the industry, lead to significant legal fees, and could result in the diversion of management's attention from managing our business.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to changes in interest rates primarily from our long-term debt arrangements and, secondarily, investments in certain short-term investments. We invest our excess cash in highly liquid short-term investments that are typically held for the duration of the term of the respective instrument. We do not utilize derivative financial instruments, derivative commodity instruments or other market risk sensitive instruments, positions or transactions to manage exposure to interest rate changes. Accordingly, we believe that, while the securities we hold are subject to changes in the financial standing of the issuer of such securities, we are not subject to any material risks arising from changes in interest rates, foreign currency exchange rates, commodity prices, equity prices or other market changes that affect market risk sensitive instruments.

ITEM 4. CONTROLS AND PROCEDURES

As of the end of the period covered by this Quarterly Report on Form 10-Q, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of March 31, 2008. There have been no significant changes in our internal controls or in other factors that could significantly affect internal controls subsequent to March 31, 2008.

An evaluation was also performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. That evaluation did not identify any change in our internal control over financial reporting that occurred during our latest fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives.

PART II – OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

On February 11, 2008 we notified Bruker Daltonics, Ibis' manufacturing and commercialization partner for the T5000 System, that we were initiating the formal dispute resolution process under our agreement with them. We have asserted that Bruker's performance of its manufacturing, commercialization and product service obligations are unsatisfactory and fail to meet their obligations under this agreement. Executive level negotiations have failed to achieve resolution of this dispute. Formal mediation efforts will be pursued immediately in an effort to avoid litigation.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Not applicable

ITEM 3. DEFAULT UPON SENIOR SECURITIES

Not applicable

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

Not applicable

ITEM 5. OTHER INFORMATION

Not applicable

ITEM 6. EXHIBITS

a. Exhibits

Exhibit Number	Description of Document
4.1	Stock Purchase Agreement between the Registrant and Genzyme Corporation dated January 7, 2008 (1).
10.1	License and Research Agreement (including Stock Purchase Agreement) between the Registrant and Genzyme Corporation dated January 7, 2008 (with certain confidential information deleted).
10.2	Amended and Restated Collaboration and License Agreement between the Registrant and Antisense Therapeutics Ltd dated February 8, 2008 (with certain confidential information deleted).
10.3	VLA4 Partner Support Agreement between the Registrant and Teva Pharmaceutical Industries Ltd dated February 8, 2008 (with certain confidential information deleted).
10.4	Strategic Alliance Master Agreement among the Registrant, Ibis Biosciences, Inc., and Abbott Molecular Inc. dated January 30, 2008 (with certain confidential information deleted).
10.5	Call Option Agreement among the Registrant, Ibis Biosciences, Inc., and Abbott Molecular Inc. dated January 30, 2008 (with certain confidential information deleted).
31.1	Certification by Chief Executive Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

31.2	Certification by Chief Financial Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

(1) Filed as part of the License and Research Agreement that is filed as Exhibit 10.1 to this Quarterly Report.

(Registrant)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
/s/ Stanley T. Crooke Stanley T. Crooke, M.D., Ph.D.	Chairman of the Board, President, and Chief Executive Officer (Principal executive officer)	May 12, 2008
/s/ B. Lynne Parshall B. Lynne Parshall, J.D.	Director, Executive Vice President, Chief Financial Officer and Secretary (Principal financial and accounting officer)	May 12, 2008

CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R §§ 200.80(b)4, AND 240.24b-2

Execution Version

LICENSE AND RESEARCH AGREEMENT

This License and Research Agreement (together with all Exhibits, Schedules and other attachments hereto, this "Agreement"), is dated as of the 7th day of January, 2008 (the "Execution Date"), by and between Genzyme Corporation, a Massachusetts corporation ("Genzyme") and Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"). Genzyme and Isis each may be referred to herein individually as a "Party" or collectively as the "Parties."

WITNESSETH:

WHEREAS, simultaneously with this Agreement, Isis and Genzyme will enter into that certain Stock Purchase Agreement of even date herewith in the form attached hereto as Exhibit A (the "Stock Purchase Agreement") pursuant to which Genzyme is purchasing the Shares;

WHEREAS, Isis possesses certain intellectual property with respect to certain oligonucleotide-based therapeutic compounds;

WHEREAS, Isis desires to grant to Genzyme, and Genzyme desires to obtain, a license under certain Isis intellectual property to advance mipomersen, formerly known as ISIS 301012, and related compounds targeting apoB, through human clinical trials and ultimately commercialize it as a product; and

WHEREAS, Isis and Genzyme desire to enter into a research agreement under which Isis will conduct research related to certain gene targets selected by Genzyme.

NOW, THEREFORE, in consideration of the Parties' willingness to enter into the Stock Purchase Agreement and the respective covenants, representations, warranties and agreements set forth herein, the Parties hereto agree as follows:

ARTICLE 1.
DEFINITIONS

For purposes of this Agreement, the following capitalized terms will have the following meanings. Capitalized terms used without definition in this Agreement will have the meanings ascribed to them in the Product Term Sheet and the Research Term Sheet.

1.1. "AAA" has the meaning set forth in Section 6.2.2 (Binding Arbitration With Respect to Agreement Terms).

1.2. "Action" has the meaning set forth in Section 6.3.1 (Jurisdiction).

1.3. "Additional Third Party Agreement" has the meaning set forth in Section 2.1.6 (Additional Rights after Effective Date).

1.4. "Affiliate" of an entity means any other entity that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such first entity. For purposes of this definition only, "control" (and, with correlative

meanings, the terms "controlled by" and "under common control with") means the possession of the actual power to direct the management or policies of an entity, whether through the ownership of voting securities or by contract relating to voting rights or corporate governance. In addition, [***] will not be considered an Affiliate of Isis.

1.5. "apoB" means apolipoprotein B.

1.6. "Bankruptcy Code" has the meaning set forth in Section 8.14 (Rights in Bankruptcy).

1.7. "Confidential Information" has the meaning set forth in Section 8.1.1 (Non-Disclosure).

1.8. "Control" or "Controlled" means, with respect to any Know-How, Patent or other intellectual property right or Regulatory Materials, possession by a Party (including its Affiliates) of the right (whether by ownership, license or otherwise) to grant to the other Party a license or a sublicense under such Know-How, Patent or other intellectual property right or access to Regulatory Materials without violating the terms of any agreement or other arrangement with any Third Party.

1.9. "Diligence Period" means the period beginning on the Execution Date and ending on the earlier of (a) the date that is [***] after the Execution Date or (b) the date the Parties enter into the More Detailed Product Agreement. The Parties' goal is to conclude diligence and enter into the More Detailed Product Agreement by [***].

1.10. "Disclosure Schedule" means the schedule (dated as of the Execution Date and updated pursuant to Section 5.4 (Right to Update Disclosure Schedule Prior to Effective Date)) delivered by Isis to Genzyme that includes exceptions to Isis' representations and warranties in Section 5.2 (Product Representations and Warranties) and Section 5.3 (Research Representations and Warranties) hereof.

1.11. "Dispute" has the meaning set forth in Section 6.1.1 (Escalation).

1.12. "Effective Date" has the meaning set forth in Section 7.1.2 (Effective Date).

1.13. "Encumbered Follow-On Product" has the meaning set forth in Section 2.2 (Follow-On Product).

1.14. "Executives" has the meaning set forth in Section 6.1.1 (Escalation).

1.15. "Follow-On Product" means all pharmaceutical compositions, formulations, dosage forms, delivery systems and presentations that contain [***] (alone or with other active ingredients) other than Mipomersen.

1.16. "Follow-On Product Encumbrances" has the meaning set forth in Section 2.2.2.

1.17. "General Representations and Warranties" has the meaning set forth in Section 5.1 (Representations and Warranties of Both Parties).

1.18. "HSR" means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended.

1.19. "In-Licensed Third Party IP" means Patents or Know-How Controlled by Isis that are in-licensed by Isis pursuant to a Third Party Agreement.

1.20. "Isis Core Technology Patents" means all Patents, other than the Product-Specific Patents or Isis Manufacturing and Analytical Patents, Controlled by Isis or any of its Affiliates as of the Execution Date hereof or during the term of the Product License that are necessary or useful for the development and commercialization of Product, including the Patents identified on Schedule 1.20.

1.21. "Isis Manufacturing and Analytical Know-How" means Know-How other than Product Know-How Controlled by Isis or its Affiliates as of the Execution Date hereof or during the term of the Product License that relates to the synthesis or analysis of Products independent of sequence or chemical modification.

1.22. "Isis Manufacturing and Analytical Patents" means Patents Controlled by Isis or its Affiliates as of the Execution Date hereof or during the term of the Product License that claim methods and materials used in the synthesis or analysis of Products independent of sequence or chemical modification, including the Patents identified on Schedule 1.22. Isis Manufacturing and Analytical Patents do not include the Product-Specific Patents and the Isis Core Technology Patents.

1.23. "Isis Manufacturing and Analytical Technology" means the Isis Manufacturing and Analytical Know-How and Isis Manufacturing and Analytical Patents solely to the extent necessary or useful to manufacture a Product.(1)

1.24. "Know-How" means technical information and materials, including technology, software, instrumentation, devices, data, compositions, formulas, biological materials, assays, constructs, compounds, discoveries, inventions, procedures, processes, practices, protocols, methods, techniques, results of experimentation or testing, knowledge, trade secrets, skill and experience, whether or not patentable or copyrightable.

1.25. "Licensed IP" means the Licensed Patents, the Product Know-How and the Isis Manufacturing and Analytical Know-How; *provided*, *however*, that (a) for any such Know-How or Patent that becomes Controlled by Isis after the Execution Date pursuant to an Additional Third Party Agreement, the provisions of Section 2.1.6 (Additional Rights after Effective Date) will govern whether such Know-How or Patent will be

(1) As part of its collaboration with other pharmaceutical partners, Isis has an arrangement where Isis can share manufacturing technology improvements made by such pharmaceutical partners with other Third Parties so long as such Third Parties similarly agree to share their manufacturing technology improvements. Genzyme may decide to participate in this arrangement if Genzyme wishes.

included as Licensed IP, and (b) with respect to any Follow-On Product, the provisions of Section 2.2 (Follow-On Product) will govern the extent to which In-Licensed Third Party IP will be included in Licensed IP.

1.26. "Licensed Patent(s)" means the Product-Specific Patents, Isis Core Technology Patents and the Isis Manufacturing and Analytical Patents.

1.27. "Mipomersen" means mipomersen sodium, formerly known as ISIS 301012.

1.28. "More Detailed Product Agreement" has the meaning set forth in Section 2.1.2 (More Detailed Product Agreement).

1.29. "More Detailed Research Agreement" has the meaning set forth in Section 2.3 (Research Option Agreement).

1.30. "Patent(s)" means (a) patents and patent applications in any country or jurisdiction, (b) all priority applications, divisionals, continuations, substitutions, and continuations-in-part of any of the foregoing, and (c) all patents issuing on any of the foregoing patent applications, together with all registrations, reissues, renewals, re-examinations, confirmations, supplementary protection certificates, and extensions of any of (a), (b) or (c).

1.31. "Permitted Licenses" means licenses granted by Isis after the Execution Date to any Third Party under the Isis Core Technology Patents or the Isis Manufacturing and Analytical Technology (but not under the Product-Specific Patents or for use of [***] to (a) use oligonucleotides (or supply oligonucleotides to end users) in quantities not to exceed [***](2) per oligonucleotide per end user solely to conduct Pre-Clinical Research, or (b) enable such Third Party to [***], where such Third Party is primarily engaged in providing contract manufacturing or services and is not engaged in drug discovery, development or commercialization. Notwithstanding the foregoing, Permitted Licenses do not include any licenses that allow (i) a Third Party to make, use or sell an oligonucleotide having the same [***] as a Product or Isis' preferred [***], (ii) a Third Party to manufacture any nucleic acid that [***] apoB that will be incorporated into a therapeutic product for use in human clinical trials or for commercial sale or (iii) Isis to directly supply to a Third Party any [***] apoB.

1.32. "Pre-Clinical Research" means pre-clinical research including gene function, gene expression and target validation research using cells and animals, which may include small pilot toxicology studies but excludes pharmacokinetic and toxicology studies

(2) Quantity subject to confirmation by the Parties during the Diligence Period.

required to meet the regulations for filing an IND, clinical development and commercialization.

1.33. "Product" means all pharmaceutical compositions, formulations, dosage forms, delivery systems and presentations that contain Mipomersen or any Follow-On Product, including all pharmaceutically acceptable salts, solvates, hydrates, hemihydrates, metabolites, pro-drug forms, stereoisomers, enantiomers, racemates and all optically active forms thereof.

1.34. "Product Know-How" means Know-How Controlled by Isis on the Execution Date or during the term of the Product License relating to or otherwise necessary for the development and commercialization of Product. Product Know-How does not include the Isis Manufacturing and Analytical Know How.

1.35. "Product License" has the meaning set forth in Section 2.1 (Grant).

1.36. "Product Representations and Warranties" has the meaning set forth in Section 5.2 (Product Representations and Warranties).

1.37. "Product-Specific Patents" means Patents Controlled by Isis or any of its Affiliates as of the Execution Date and during the term of the Product License claiming or covering (a) [***] apoB; (b) the sequence of apoB; (c) the specific composition of matter of a Product; and (d) methods of using Product as a therapeutic, methods of using Product to modulate apoB, and methods of using the product to inhibit expression of apoB, including the Patents identified on Schedule 1.37; *provided*, *however*, that if a Patent satisfies the criteria set forth above but also applies to gene targets other than apoB, such Patent will be considered an Isis Core Technology Patent.

1.38. "Product Term Sheet" means the term sheet attached hereto as Exhibit B.

1.39. "Regulatory Materials" means any regulatory submissions, notifications, registrations, approvals and/or other filings and correspondence made to or with a regulatory authority in any country or jurisdiction in the Territory, and any other records required to be maintained for possible audit by a regulatory authority that may be necessary or useful to develop, manufacture, market, sell or otherwise commercialize Product in the Territory.

1.40. "Research Option Agreement" has the meaning set forth in Section 2.3 (Research OptionAgreement).

1.41. "Research Term Sheet" means the term sheet attached hereto as Exhibit C.

1.42. "SEC" means Securities and Exchange Commission.

1.43. "Shares" means the shares of Isis' Common Stock purchased by Genzyme pursuant to the Stock Purchase Agreement.

1.44. "Territory" means worldwide.

1.45. "Third Party" means a person or entity other than the Parties and their respective

Affiliates.

1.46. "Third Party Agreement" means any agreements pursuant to which Isis obtains rights applicable to the development or commercialization of Product or Follow-On Product.

ARTICLE 2.
LICENSE AND RESEARCH AGREEMENTS

2.1. Product License.

2.1.1. Grant. Isis hereby grants to Genzyme an exclusive license, (with the limited right to sublicense as set forth in Section 2.1.3 (Limited Right to Sublicense)), under the Licensed IP to research, develop, make, have made, use, sell, offer for sale, have sold, import and export Products in the Territory for therapeutic purposes on the terms and conditions set forth in the Product Term Sheet and this Agreement (the "Product License"). Notwithstanding the foregoing, (a) the exclusive license to the Isis Core Technology Patents will be subject to the licenses granted by Isis to Third Parties identified on Schedule 2.1.1 and Isis' right to grant Permitted Licenses, and (b) with respect to any Follow-On Product, the provisions of Section 2.2 (Follow-On Product) will govern the extent to which In-Licensed Third Party IP is included within Licensed IP.

2.1.2. More Detailed Product Agreement. The Parties agree that the Product Term Sheet and this Agreement contain all material terms of the Product License and will form a legally binding and enforceable license and co-development agreement without need for execution of further documentation or any further action by any Party. The Parties also recognize that it may be desirable to agree upon other more detailed customary terms and conditions with respect to the Product License. Accordingly, as soon as reasonably practicable after the Effective Date, the Parties will negotiate and enter into a more detailed written license and co-development agreement that will include the terms set forth in the Product Term Sheet and any additional terms and conditions that are customary and reasonable for agreements of this

type that may be agreed to by the Parties, including provisions relating to intellectual property ownership, prosecution and enforcement, regulatory interactions and approvals, term and termination, indemnification and confidentiality (the "More Detailed Product Agreement").

2.1.3. Limited Right to Sublicense.

(a) The licenses granted to Genzyme under the Licensed IP are sublicensable only in connection with a sublicense of a Product to any Affiliate of Genzyme or to any Third Party, in each case for the continued research, development or commercialization of such Product in accordance with the terms of the Product License.

(b) Notwithstanding the foregoing, the licenses granted to Genzyme under the Isis Manufacturing and Analytical Technology are sublicensable to a Third Party [***] only upon the mutual agreement of the Parties.

2.1.4. Upfront License Fee. Provided that this Agreement and the Product License have become effective and neither has not been terminated, Genzyme will pay to Isis the upfront license fee specified in the Product Term Sheet upon five (5) business days after the earlier of (a) expiration of the Diligence Period or (b) the Parties enter into the More Detailed Product Agreement.

2.1.5. Access. Isis will afford to Genzyme and its representatives reasonable access to and copies of all information (including reasonable access to knowledgeable employees and representatives of Isis to discuss such information) within the possession or control of Isis or any of its Affiliates pertaining to the development of the Product and the Licensed IP, including all Regulatory Materials related to the Product.

2.1.6. Additional Rights after Effective Date. After the Execution Date, Isis may wish to in-license or acquire rights to Know-How or Patents Controlled by Third Parties (such a Third Party in-license or acquisition agreement being an "Additional Third Party Agreement") which, if so licensed or acquired, may be included in the Licensed IP licensed to Genzyme under Section 2.1.1. In such event (and to the extent permitted by Isis' confidentiality agreement with the applicable Third Party), Isis will notify Genzyme regarding the nature of the technology and status of negotiations related to the Additional Third Party Agreement through the JDC. Once Isis has executed such Additional Third Party Agreement, Isis will offer such Third Party Patents or Know-How to Genzyme (which offer will include a description of the payments paid or potentially payable by Isis thereunder). At such time, if Genzyme wishes to include such Third Party Patents or Know-How under the licenses granted under Section 2.1.1, Genzyme will notify Isis of its desire to do so and the Parties will fairly and in good faith allocate upfront payments or ongoing payment obligations between Products and compounds that are not Products and other Isis licensees, if appropriate. As part of this allocation process, Isis will share with Genzyme, in reasonable detail, the assumptions and methodology Isis used to create the proposed allocation. If Genzyme does not agree to reimburse Isis for the amount of any upfront or similar acquisition payments fairly allocated to Product, and to be responsible for the payment of its share of any upfront, milestone and royalty payments, then the Know-How or Patents acquired or in licensed by Isis under the Additional Third Party Agreement will not be considered Licensed IP licensed to Genzyme under the Product License. When Genzyme pays its share of any upfront, milestone and royalty payments assumed by Genzyme under this Section 2.1.6, such payments will be considered Program Costs for the applicable Product.

2.2. Follow-On Product. The Parties contemplate that after the Effective Date Genzyme, either on its own or in collaboration with Isis, may wish to research, develop and commercialize Follow-On Products. The scope of the In-Licensed Third Party IP included in Licensed IP under the Product License with respect to such Follow-On Products will be determined in accordance with the procedures set forth in this Section 2.2. At the time Genzyme intends to designate a Follow-On Product as a development candidate, Genzyme will notify Isis in writing of such intention and will describe in

reasonable detail the applicable Follow-On Product. Subject to Section 2.1.6 (Additional Rights after Effective Date), if a Follow-On Product utilizes any In-Licensed Third Party IP (an "Encumbered Follow-On Product"), such In-Licensed Third Party IP will be included in Licensed IP only to the extent set forth below:

2.2.1. If the applicable Third Party Agreement contains a contractual obligation that would preclude Isis from including such In-Licensed Third Party IP in Licensed IP with respect to such Encumbered Follow-On Product, then the In-Licensed Third Party IP that is the subject of such Third Party Agreement will not be included in Licensed IP.

2.2.2. If the applicable Third Party Agreement contains any potential encumbrances known by Isis and related to the potential Follow-On Product, including field or territory restrictions, covenants, or milestones, royalty, sublicense revenue or other payments ("Follow-On Product Encumbrances"), Isis will fully disclose to Genzyme such Follow-On Product Encumbrances and, if Genzyme agrees in writing to assume the Follow-On Product Encumbrances (with any payments being included in Program Costs for such Encumbered Follow-On Product), then the In-Licensed Third Party IP that is the subject of such Third Party Agreement will be included in Licensed IP.

2.2.3. If the applicable Third Party Agreement does not contain the obligations or encumbrances described in Sections 2.2.1 and 2.2.2 above, the In-Licensed Third Party IP that is the subject of such Third Party Agreement will automatically be included in Licensed IP.

2.2.4. If the applicable Third Party Agreement is or was also applicable to Mipomersen, then the In-Licensed Third Party IP that is the subject of such Third Party Agreement will automatically be included in the Licensed IP to the extent that (a) the terms of such Third Party Agreement do not preclude Isis from including it and (b) Genzyme agrees in writing to assume any applicable Follow-On Product Encumbrances associated with such Third Party Agreement.

2.2.5. Each time the Parties complete the process set forth above, Isis will update the schedules relating to Licensed Patents and Third Party Agreements, and Schedule 2.1.1 as appropriate.

2.3. Research Option Agreement. Isis and Genzyme hereby enter into a research agreement under which Isis will perform research on the terms and conditions set forth in the Research Term Sheet (the "Research Option Agreement"). The Parties agree that the Research Term Sheet and this Agreement contain all material terms of the Research Option Agreement and will form a legally binding and enforceable research agreement, without need for execution of further documentation or any further action by any Party. The Parties also recognize that it may be desirable to agree upon other more detailed customary terms and conditions with respect to the Research Option Agreement. Accordingly, as quickly as practicable following the Effective Date, the Parties will negotiate and enter into a more detailed research agreement that will include the terms set

forth in the Research Term Sheet and any additional terms and conditions that are customary and reasonable for agreements of this type that may be agreed to by the Parties, including provisions relating to intellectual property ownership, prosecution and enforcement, regulatory matters, term and termination, indemnification and confidentiality (the "More Detailed Research Agreement").

ARTICLE 3.
NON-COMPETE

3.1. Product. During the term of the Product License, Isis and its Affiliates will not, directly or indirectly, and will not collaborate with, license or otherwise authorize any Third Party to, research, develop or commercialize any [***] apoB, except pursuant to (a) the agreements identified on Schedule 2.1.1, as they exist on the Execution Date, (b) Permitted Licenses, or (c) this Agreement, including the Product License, and the More Detailed Product Agreement.

ARTICLE 4.
[RESERVED]

ARTICLE 5.
REPRESENTATIONS AND WARRANTIES

5.1. Representations and Warranties of Both Parties. Each Party hereby represents and warrants to the other Party as of both the Execution Date and Effective Date (collectively, the "General Representations and Warranties") that:

5.1.1. it is a duly organized and validly existing corporation under the laws of its jurisdiction of incorporation;

5.1.2. it has the power and authority and the legal right to enter into this Agreement and perform its obligations hereunder, and that it has taken all necessary action on its part required to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder;

5.1.3. the execution and delivery of this Agreement, the Product License and the Research Option Agreement and the performance of such Party's obligations hereunder do not conflict with or violate any requirement of applicable law or any provision of its articles of incorporation or similar organizational documents, its bylaws, or the terms or provisions of any agreement or other instrument to which it is a party or by which it is bound, or any order, award, judgment or decree to which it is a party or by which it is bound; and

5.1.4. this Agreement has been duly executed and delivered on behalf of such Party and constitutes a legal, valid and binding obligation of such Party and is enforceable against it in accordance with its terms subject to the effects of bankruptcy, insolvency or other laws of general application affecting the enforcement of creditor rights and judicial principles affecting the availability of specific performance and general principles of equity, whether enforceability is considered

a proceeding at law or equity.

5.2. Product Representations and Warranties. Isis represents and warrants to Genzyme that the statements contained in this Section 5.2 (the "Product Representations and Warranties") are true and correct as of the Execution Date and will be true as of the Effective Date, as though made as of the Effective Date, with each such representation and warranty subject only to such exceptions, if any, as are set forth in the particular section in the Disclosure Schedule attached hereto as Exhibit D that corresponds to the particular section number in this Agreement:

5.2.1. Schedule 1.20, Schedule 1.22, and Schedule 1.37 set forth true, correct and complete lists of all Isis Core Technology Patents, Isis Manufacturing and Analytical Patents, and Product-Specific Patents, respectively, and all Licensed Patents used in the development or commercialization of Mipomersen and existing as of the Execution Date and indicates whether each such Patent is owned by Isis or licensed by Isis from a Third Party and if so, identifies the licensor or sublicensor from which the Patent is licensed.

5.2.2. A true, correct and complete list of any Third Party Agreements related to Mipomersen is set forth on Schedule 5.2.2.

5.2.3. With respect to all Product-Specific Patents, and all Licensed IP used in the development or commercialization of Mipomersen, Isis has the sufficient legal and/or beneficial title and ownership or rights to grant the Product License to Genzyme and the grant of the Product License to Genzyme does not violate the terms of any Third Party Agreement or any other agreement Isis has with a Third Party.

5.2.4. Each of the Product-Specific Patents, and each of the Licensed Patents used in the development or commercialization of Mipomersen properly identifies each and every inventor of the claims thereof as determined in accordance with the laws of the jurisdiction in which such Patent is issued or such application is pending.

5.2.5. With respect to all Product-Specific Patents owned by Isis, and all Licensed Patents owned by Isis and used in the development or commercialization of Mipomersen, (a) each person who has or has had any rights in or to each of such Patents has executed an agreement

assigning his, her or its entire right, title and interest in and to such Patents to Isis and (b) to the best of Isis' knowledge, each such inventor has complied in all material respects with all applicable duties of candor and good faith in dealing with any patent office, including the duty to disclose to any applicable patent office all information known to be material to patentability.

5.2.6. To the best of Isis' knowledge, no circumstances or grounds exist that would invalidate, reduce or eliminate, in whole or in part, the enforceability, validity or scope of any Product-Specific Patent or any Licensed Patent used in the development or commercialization of Mipomersen.

5.2.7. Isis is not aware of any Patents owned or Controlled by a Third Party that would be infringed by Genzyme during the development or commercialization of Mipomersen in its current form.

5.2.8. To the best of Isis' knowledge, no actions, suits, claims, disputes or proceedings concerning the Licensed Patents are currently pending or are threatened, that if determined adversely to Isis would have a material adverse effect on or would impair Genzyme's rights under the Product License.

5.2.9. Isis is not subject to any agreement with any Third Party or to any outstanding order, judgment or decree of any court or administrative agency that restricts it in any way from granting to Genzyme the Product License.

5.2.10. Isis has not granted, or permitted to be attached, and it will not grant or permit to be attached, any lien, security interest or other encumbrance with respect to any Product-Specific Patent, or any Licensed IP used in the development or commercialization of Mipomersen which would adversely affect the rights granted to Genzyme hereunder.

5.2.11. Each Third Party Agreement related to Mipomersen is in full force and effect, and Isis, and to the best of Isis' knowledge, each counterparty thereto, is in compliance in all material respects with all such Third Party Agreements and no circumstances or grounds exist that would reasonably be expected to give rise to a claim of material breach or right of rescission, termination, revision or amendment of such Third Party Agreements.

5.2.12. Isis has not assigned, licensed, sublicensed, granted any interest in or options to, or entered into an agreement with respect to the Licensed IP with a Third Party that would adversely impair Genzyme's exclusive rights under this Agreement, except for the agreements identified on Schedule 2.1.1.

5.2.13. Isis has not received any claim alleging that Isis' development of Mipomersen or use of any Product-Specific Patent or any Licensed IP used in the development or commercialization of Mipomersen interferes with, infringes, or misappropriates any intellectual property rights of any Third Party (including any claim that Isis must license or refrain from using any intellectual property rights of any Third Party in order to develop, make, use, sell or offer for sale any product or technology using or incorporating the Licensed IP), and to the best of Isis' knowledge, the development and commercialization of Mipomersen and the use of any Product-Specific Patent or any Licensed IP used in the development or commercialization of Mipomersen will not interfere with, infringe or misappropriate the intellectual property rights of any Third Party. To the best of Isis' knowledge, no Third Party has interfered with, infringed upon or misappropriated the Licensed IP in the making, using or selling of a lipid lowering product.

5.2.14. Isis holds, and is operating in material compliance with, such exceptions, permits,

licenses, franchises, authorizations and clearances of any governmental entity required in connection with the current development of Mipomersen. Isis has not received any warning letters or written correspondence from any governmental entity requiring the termination, suspension or modification of any clinical or pre-clinical studies or tests with respect to Mipomersen. Isis has conducted and required its contractors to conduct all clinical studies related to Mipomersen in accordance with cGCP, cGLP and applicable law.

5.2.15. As of the Execution Date, Isis has prepared, maintained and retained all Regulatory Materials required to be maintained or reported pursuant to and in accordance with applicable laws and the Regulatory Materials do not contain any materially false or misleading statements.

5.2.16. Except for the agreements identified on Schedule 2.1.1, Isis has not granted to any Third Party rights under the Licensed Patents to research, develop or commercialize any nucleic acid that hybridizes to a nucleic acid molecule encoding apoB.

5.3. Research Representations and Warranties. Isis represents and warrants to Genzyme that the statements contained in this Section 5.3 are true and correct as of the Execution Date and will be true as of the Effective Date, as though made as of the Effective Date, with each such representation and warranty subject only to such exceptions, if any, as are set forth in the particular section in the Disclosure Schedule attached hereto as Exhibit D that corresponds to the particular section number in this Agreement:

5.3.1. To the best of Isis' knowledge, no actions, suits, claims, disputes or proceedings are currently pending or are threatened, that if determined adversely to Isis would have a material adverse effect on or impair Isis' ability to perform its obligations under the Research Option Agreement.

5.3.2. Isis is not subject to any agreement with any Third Party or to any outstanding order, judgment or decree of any court or administrative agency that materially restricts Isis from performing its obligations under the Research Option Agreement.

5.3.3. Isis has sufficient resources to perform the activities contemplated under the Research Option Agreement and the Isis personnel or permitted contractors performing such activities will be skilled, appropriately credentialed, licensed and qualified to provide the specific research services they are providing.

5.4. Right to Update Disclosure Schedule Prior to Effective Date. On or before the Effective Date, Isis may deliver to Genzyme an updated Disclosure Schedule reflecting any exceptions to the representations and warranties made by Isis as of the Effective Date.

5.5. Isis Covenants.

5.5.1. Third Party Agreements. Isis covenants that it will not, without Genzyme's prior written consent, agree, consent or acquiesce to any amendment, supplement or

other modification to any Third Party Agreement or take any action under such Third Party Agreement or with respect to the intellectual property licensed thereunder that would adversely affect the rights granted to Genzyme under this Agreement, including under the Product License.

5.5.2. Sublicense Survival. Isis covenants that it will use good faith and commercially reasonable efforts to enter into any necessary amendments or side agreements to its Third Party Agreements to ensure that (a) sublicenses under each Third Party Agreement will survive termination of such Third Party Agreement or (b) Genzyme will receive a direct license from the counterparty to each Third Party Agreement upon termination of such Third Party Agreement.

5.5.3. Notice of Developments. During the Diligence Period, Isis will give Genzyme prompt written notice upon becoming aware of any development, event or circumstance that could reasonably be expected to result in a breach of or inaccuracy in any of the General Representations and Warranties and Product Representations and Warranties.

ARTICLE 6.
DISPUTE RESOLUTION

6.1. Escalation.

6.1.1. In the event any dispute, controversy or claim arises under, out of, in connection with or in relation to this Agreement, or the breach, termination, validity or enforceability of any provision hereof (a "Dispute"), the Parties will discuss and negotiate in good faith a solution acceptable to the Parties and in the spirit of this Agreement. If, after negotiating in good faith pursuant to the foregoing sentence, the Parties fail to reach agreement within sixty (60) days, then the Dispute may be referred to the Chief Executive Officer of Genzyme and the Chief Executive Officer of Isis (the "Executives") for resolution at the request of either Party.

6.1.2. If the Executives fail, after good faith discussions, to reach an amicable agreement on the Dispute within ten (10) business days of submission to the Executives, then:

(a) if the Dispute relates to the Parties' failure to reach agreement with respect to the interpretation of this Agreement, the Product Term Sheet or Research Term Sheet or with respect to any term or condition to be included in the More Detailed Product Agreement or More Detailed Research Agreement, then either Party's sole recourse is to submit such Dispute to binding arbitration pursuant to Section 6.2 (Binding Arbitration with Respect to Agreement Terms) after providing written notice to the other Party; and

(b) if the Dispute relates to any other matter, either Party may pursue a legal remedy in accordance with Section 6.3 (Jurisdiction, Venue, Service of Process).

6.2. Binding Arbitration With Respect to Agreement Terms.

6.2.1. If the Parties fail to reach agreement with respect to the interpretation of this Agreement, the Product Term Sheet or Research Term Sheet or with respect to any term or condition to be included in the More Detailed Product Agreement or More Detailed Research Agreement and the Dispute is not resolved informally through negotiation between the Parties or the Executives, then the Dispute will be submitted to binding arbitration. The Parties will select a mutually agreeable arbitrator experienced in matters regarding contracts of a similar nature who (a) is a lawyer with at least fifteen (15) years experience who has extensive experience negotiating and drafting license, research and collaboration agreements among biotechnology and pharmaceutical companies and (b) has no affiliation or pre-existing relationship with either Genzyme or Isis or their respective Affiliates. If the Parties are unable to agree on an arbitrator within a thirty (30) day period, then each Party will select an arbitrator satisfying the criteria described in the immediately preceding sentence within five (5) business days, the two (2) designated arbitrators will select a mutually agreeable third arbitrator satisfying the criteria described in the immediately preceding

sentence within five (5) business days and all three (3) arbitrators will hear the Dispute as a panel and render a decision upon the determination of the majority of the panel. In each case, the arbitrator(s) will render their decision by supplying the term or condition upon which the Parties failed to agree.

6.2.2. The arbitration will be conducted in accordance with the rules of, and under the auspices of, the American Arbitration Association (the "AAA"). The decisions rendered by the arbitrators will be final and binding, and the Parties will not have any right of appeal to any court on the merits of the Dispute. Judgment upon the award rendered in any such arbitration may be entered in any court having jurisdiction thereof. The location of the arbitration will be Chicago, Illinois. This Agreement and the Product License and Research Option Agreement will remain in effect pending completion of the proceedings brought under this Section 6.2. Each Party will bear its own costs and expenses with respect to any such arbitration, including one-half of the fees and expenses of the arbitrator.

6.3. Jurisdiction; Venue; Service of Process.

6.3.1. Jurisdiction. Each Party by its execution hereof, (a) hereby irrevocably submits to the exclusive jurisdiction of the United States District Court located in Chicago, Illinois for the purpose of any Dispute arising between the Parties in connection with this Agreement, other than those Disputes that must be resolved by binding arbitration pursuant to Section 6.2 (Binding Arbitration With Respect to Agreement Terms) (each, an "Action"), and (b) hereby waives to the extent not prohibited by applicable law, and agrees not to assert, by way of motion, as a defense or otherwise, in any such Action, any claim that it is not subject personally to the jurisdiction of the above-named court, that its property is exempt or immune from attachment or execution, that any such Action brought in the above-named court should be dismissed on grounds of forum non conveniens,

should be transferred or removed to any court other than the above-named court, or should be stayed by reason of the pendency of some other proceeding in any other court other than the above-named court, or that this Agreement or the subject matter hereof may not be enforced in or by such court and (c) hereby agrees not to commence any such Action other than before the above-named court. Notwithstanding the previous sentence a Party may commence any Action in a court other than the above-named court solely for the purpose of enforcing an order or judgment issued by the above-named court.

6.3.2. Venue. Each Party agrees that for any Action between the Parties arising in whole or in part under or in connection with this Agreement, such Party bring Actions only in the federal courts of the United States of America located in Chicago, Illinois and any appellate court having jurisdiction over appeals from such courts. Each Party further waives any claim and will not assert that venue should properly lie in any other location within the selected jurisdiction.

6.3.3. Service of Process. Each Party hereby agrees that service of process made by registered or certified mail, return receipt requested, at its address specified pursuant to Section 8.5 (Notices), will constitute good and valid service of process in any such Action and (c) waives and agrees not to assert (by way of motion, as a defense, or otherwise) in any such Action any claim that service of process made in accordance with clause (a) or (b) does not constitute good and valid service of process.

ARTICLE 7.
CONDITIONS PRECEDENT AND TERMINATION

7.1. Conditions Precedent.

7.1.1. HSR Compliance.

(a) Each Party will use commercially reasonable efforts to satisfy any applicable requirements under the HSR, and the regulations promulgated thereunder, including by making an initial HSR filing no later than five (5) days after the Execution Date or upon such other timing as mutually agreed by the Parties.

(b) Each Party will cooperate with the other Party in the prompt preparation, execution and filing of all documents that are required or permitted to be filed pursuant to HSR, and to notify the other Party upon receipt of any formal or informal requests for information from any government agency in connection with any filings under HSR. Each Party will bear its own costs with respect thereto (except the filing fees for HSR, which will be paid by Genzyme).

7.1.2. Effective Date. This Agreement will not be effective until the date (the "Effective Date") the requirements described in Section 7.1.1 have been satisfied and all applicable waiting periods (including any extensions thereof) under HSR have

expired or been terminated. All obligations, rights, duties and liabilities under this Agreement (except those contained in this Section 7.1 (Conditions Precedent), Article 3 (Non-Compete), Article 5 (Representations and Warranties) and Article 8 (Miscellaneous) of this Agreement) are subject to such date.

7.1.3. Party's Termination Right. If the Effective Date has not occurred within ninety (90) days after the Execution Date, notwithstanding that each Party has fulfilled its obligations under this Section 7.1, either Party has the right to terminate this Agreement without liability to the other Party by notice in writing with immediate effect; *provided, however*, that if the Parties receive a request for more information from a

government agency in connection with the HSR filing, the Parties will mutually agree to extend the ninety (90) day period for a reasonable period of time.

7.2. Isis' Right to Terminate. If either (a) after the satisfaction or waiver of the closing conditions set forth in Section 5.2 of the Stock Purchase Agreement, Genzyme has not paid Isis the Purchase Price for the Shares by the Closing Date (as required by and defined in the Stock Purchase Agreement) or (b) Genzyme fails to pay the upfront license fee when due under Section 2.1.4 (Upfront License Fee), Isis has the right to terminate this Agreement without liability to Genzyme by notice in writing with immediate effect if Genzyme has failed to cure such non-payment within a reasonable period of time after receiving written notice from Isis of such failure to pay.

7.3. Termination by Genzyme. The Parties have negotiated and entered into this Agreement (but not the Stock Purchase Agreement) on an abbreviated schedule that has not permitted Genzyme to complete a customary due diligence review and analysis of the Product's clinical data, regulatory history, relevant Isis and Third Party intellectual property, and relevant Third Party Agreements, and intend for Genzyme to conduct and complete such a due diligence review and analysis during the Diligence Period. Therefore, Genzyme may terminate the Product License with immediate effect by providing written notice to Isis at any time during the Diligence Period if, based on its due diligence review and analysis, Genzyme concludes in good faith that the value of the Product License is significantly reduced. For purposes of clarification, this Section 7.3 does not give Genzyme the right to terminate the Stock Purchase Agreement.

ARTICLE 8.
MISCELLANEOUS

8.1. Confidentiality.

8.1.1. Non-Disclosure. Genzyme and Isis agree that all information relating to the Licensed IP, the terms and conditions of this Agreement (including the Product Term Sheet and Research Term Sheet), or any activities conducted in connection with or pursuant to this Agreement and disclosed by either Party in accordance with this Agreement ("Confidential Information") will be used and disclosed by the receiving Party only to perform its obligations and exercise its rights under this Agreement. Information relating to the development of the Product, the Licensed IP and the terms and conditions of this Agreement will be considered the Confidential Information of both Parties under the Agreement, as if both Parties were receiving Parties. Notwithstanding the foregoing, "Confidential Information" will not include information that the receiving Party can establish:

(a) was already known by the receiving Party (other than under an obligation of confidentiality) at the time of disclosure by the disclosing Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure or development, as the case may be, other than through any act or omission of the receiving Party or any of its Affiliates;

(d) was disclosed to the receiving Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the disclosing Party not to disclose such information to others; or

(e) was independently discovered or developed by or on behalf of the receiving Party without the use of any Confidential Information belonging to the disclosing Party.

8.1.2. Authorized Disclosure and Use. Notwithstanding the foregoing provisions of Section 8.1.1, each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary to:

(a) prosecute or defend litigation,

(b) comply with applicable governmental laws and regulations (including the rules and regulations of the SEC); or

(c) make filings and submissions to, or correspond or communicate with, any government authority.

In the event a Party deems it reasonably necessary to disclose Confidential

Information belonging to the other Party pursuant to clauses (a), (b) and (c) of this Section 8.1.2, the disclosing Party will to the extent possible give reasonable advance notice of such disclosure to the other Party and take reasonable measures to ensure confidential treatment of such information.

8.2. Specific Performance. Each Party acknowledges and agrees that, in the event of any breach of this Agreement by such Party or any of its Affiliates, the non-breaching Party may be irreparably and immediately harmed and may not be able to be made whole by monetary damages. Without

prejudice to any rights and remedies otherwise available, the non-breaching Party will be entitled to seek equitable relief by way of injunction, specific performance or otherwise if the breaching Party or any of its Affiliates breaches any provision of this Agreement.

8.3. Governing Law. This Agreement will be governed by and interpreted in accordance with the laws of the State of New York without reference to its choice of laws or conflicts of laws provisions.

8.4. Waiver. The failure by either Party to take any action or assert any right hereunder will in no way be construed to be a waiver of such right, nor in any way be deemed to affect the validity of this Agreement or any part hereof, or the right of a Party to thereafter enforce each and every provision of this Agreement.

8.5. Notices. Any consent or notice required or permitted to be given or made under this Agreement by one of the Parties hereto to the other will be in writing and delivered by hand or sent by nationally recognized overnight delivery service, prepaid registered or certified air mail, or by facsimile confirmed by prepaid, registered or certified mail letter, and will be deemed to have been properly served to the addressee upon receipt of such written communication, in any event to the following addresses (or any updated address provided to the notifying Party in writing in accordance with this Section 8.5):

If to Genzyme:	Genzyme Corporation 500 Kendall Street Cambridge, Massachusetts 02142 Attn: General Manager, Cardiovascular Business Unit Fax: (617) 252-7553
with a copy to:	Genzyme Corporation 500 Kendall Street Cambridge, Massachusetts 02142 Attn: General Counsel Fax: (617) 252-7553
If to Isis:	Isis Pharmaceuticals, Inc. 1896 Rutherford Road Carlsbad, CA 92008 Attn: COO and CFO

Fax: (760) 603-4650

with a copy to:	Isis Pharmaceuticals, Inc. 1896 Rutherford Road Carlsbad, CA 92008 Attn: General Counsel Fax: (760) 268-4922

8.6. Entire Agreement. This Agreement and all Exhibits and Schedules attached hereto (the terms of which are incorporated herein by reference) sets forth all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes and terminates all prior agreements (including the Confidential Disclosure and Standstill Agreement dated September 19, 2007 between the Parties) and understandings between the Parties and constitutes the entire agreement between the Parties with respect to the subject matter hereof. All Exhibits and Schedules referred to herein and other attachments hereto are intended to be, and hereby are, specifically incorporated herein and made a part of this Agreement. No subsequent alteration, amendment or modification to this Agreement will be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

8.7. Binding Effect; Assignment. This Agreement will inure to the benefit of and be binding upon the Parties and their respective successors and permitted assigns. Neither Party will assign this Agreement or any of its rights or obligations hereunder without the prior written consent of the other Party; *provided*, *however*, that Genzyme may assign this Agreement or its rights or obligations hereunder to any of its Affiliates.

8.8. Press Releases. Except as required by applicable law, neither Party will give notice to any Third Party or otherwise make any public statement or releases concerning this Agreement or the transactions contemplated hereby without obtaining the prior written consent of the other Party to this Agreement as to the contents and manner of presentation and publication thereof, which consent will not be unreasonably withheld, delayed or conditioned.

8.9. Severability. If any term, covenant or condition of this Agreement or the application thereof to any Party or circumstance, to any extent, is invalid or unenforceable, then (a) the remainder of this Agreement, or the application of such term, covenant or condition to Parties or circumstances other than those as to which it is invalid or unenforceable, will not be affected thereby and each term, covenant or condition of this Agreement will be valid and be enforced to the fullest extent permitted by law; and (b) the Parties hereto covenant and agree to renegotiate any such term, covenant or application thereof in good faith in order to provide a reasonably acceptable alternative to the term, covenant or condition of this Agreement or the application thereof that is invalid or unenforceable, it being the intent of the Parties that the basic purposes of this Agreement are to be effectuated.

8.10. Further Assurances. Each Party will execute such other instruments, give such further

assurances and perform such acts which are or may become necessary or appropriate to effectuate and carry out the provisions and intent of this Agreement.

8.11. Independent Contractors. The status of the Parties under this Agreement will be that of independent contractors. No Party will have the right to enter into any agreements on behalf of the other Party, nor will it represent to any Third Party that it has any such right or authority. Nothing in this Agreement will be construed as establishing a partnership or joint venture relationship between the Parties hereto.

8.12. Interpretation. The article and section headings herein are for reference purposes only and will not affect the meaning or interpretation hereof. The term "including" (or any variation thereof such as "include") will be without limitation.

8.13. Counterparts. This Agreement may be executed in one or more counterpart copies, and by facsimile signature, each of which will be deemed an original and all of which taken together will be deemed to constitute one and the same instrument.

8.14. Rights in Bankruptcy. All rights and licenses now or hereafter granted under or pursuant to this Agreement, the Product Term Sheet and the Research Term Sheet, including Section 2.1 of this Agreement, are rights to "intellectual property" (as defined in Section 101(35A) of Title 11 of the United States Code, as amended (such Title 11, the "Bankruptcy Code")). Isis hereby grants to Genzyme and all Affiliates of Genzyme a right of access and to obtain possession of and to benefit from (a) copies of research data, (b) laboratory samples, (c) samples of Product, (d) formulas, (e) laboratory notes and notebooks, (f) data and results related to clinical trials, (g) regulatory filings and approvals, (h) rights of reference in respect of regulatory filings and approvals, (i) pre-clinical research data and results, and (j) marketing, advertising and promotional materials, all of which constitute "embodiments" of intellectual property pursuant to Section 365(n) of the Bankruptcy Code, and (k) all other embodiments of such intellectual property, in each case, solely in connection with Genzyme's rights under the Product License and the Research Option Agreement, whether any of the foregoing are in Isis' possession or control or in the possession and control of Third Parties. Isis agrees not to interfere with Genzyme's and its Affiliates' exercise of rights and licenses to intellectual property licensed hereunder and embodiments thereof in accordance with this Agreement and agrees to use commercially reasonable efforts to assist Genzyme and its Affiliates to obtain such intellectual property and embodiments thereof in the possession or control of Third Parties as reasonably necessary or desirable for Genzyme or its Affiliates to exercise such rights and licenses in accordance with this Agreement. The Parties hereto acknowledge and agree that all payments by Genzyme to Isis in the Product Term Sheet, other than the Profit Sharing and Sales Milestones referred to in the Product Term Sheet, do not constitute "royalties" within the meaning of Bankruptcy Code §365(n) or relate to licenses of intellectual property hereunder.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the Parties have caused this License and Research Agreement to be executed by their officers thereunto duly authorized as of the date first written above.

Genzyme Corporation

By: /s/ Earl M. Collier, Jr.
Name: Earl M. Collier, Jr.
Title: EVP

Isis Pharmaceuticals, Inc.

By: /s/ B. Lynne Parshall
Name: B. Lynne Parshall
Title: COO & CFO

SCHEDULE 1.20

ISIS CORE TECHNOLOGY PATENTS
[***]

SCHEDULE 1.22

ISIS MANUFACTURING & ANALYTICAL PATENTS
[***]

SCHEDULE 1.37

PRODUCT-SPECIFIC PATENTS
[***]

Schedule 2.1.1

Licenses to Third Parties
[***]

2

Schedule 5.2.2

Third Party Agreements
[***]

Exhibit A

Stock Purchase Agreement

Execution Version

STOCK PURCHASE AGREEMENT

THIS STOCK PURCHASE AGREEMENT (***"Agreement"***) is entered into as of January 7, 2008, by and between **GENZYME CORPORATION**, a Massachusetts corporation (***"Genzyme"***), and **ISIS PHARMACEUTICALS, INC.**, a Delaware corporation (***"Isis"***).

RECITALS

A. Isis has agreed to sell, and Genzyme has agreed to purchase, shares of Isis' common stock (the ***"Common Stock"***) subject to and in accordance with the terms and provisions hereof.

B. Isis and Genzyme are entering into a License and Research Agreement, dated the same date hereof (the ***"License and Research Agreement"***).

C. The capitalized terms used herein and not otherwise defined have the meanings given to them in Appendix 1.

AGREEMENT

For good and valuable consideration, the Parties agree as follows:

SECTION 1. SALE AND PURCHASE OF STOCK

1.1 Purchase of Stock. Subject to the terms and conditions of this Agreement, at the Closing, Isis will issue and sell to Genzyme, and Genzyme will purchase from Isis, 5,000,000 shares of Common Stock (the ***"Shares"***) for an aggregate purchase price of $150,000,000 (the ***"Purchase Price"***).

1.2 Payment. At the Closing, Genzyme will pay the Purchase Price by wire transfer of immediately available funds in accordance with wire instructions provided by Isis to Genzyme prior to the Closing, and Isis will deliver a stock certificate representing the Shares to Genzyme.

1.3 Closing. The closing of the transactions contemplated by this Section 1 (the ***"Closing"***) will be held at the offices of Isis within three Business Days after the conditions to closing set forth in Section 5 are satisfied or waived (other than those conditions that by their nature are to be satisfied or waived at the Closing) or at such other place, time and/or date as may be jointly designated by Genzyme and Isis (the ***"Closing Date"***).

SECTION 2. REPRESENTATIONS AND WARRANTIES OF ISIS

Except as otherwise specifically contemplated by this Agreement, Isis hereby represents and warrants to Genzyme that:

2.1 Organization and Qualification. Isis is duly incorporated, validly existing and in good standing under the laws of the State of Delaware, with full corporate power and authority to conduct its business as currently conducted as disclosed in the SEC Documents. Isis is duly qualified to do business and is in good standing in every jurisdiction in which the nature of the

business conducted by it or property owned by it makes such qualification necessary, except where the failure to be so qualified or in good standing, as the case may be, would not reasonably be expected to have a Material Adverse Effect.

2.2 Authorization; Enforcement. Isis has all requisite corporate power and authority to enter into and to perform its obligations under this Agreement, to consummate the transactions contemplated hereby and to issue the Shares in accordance with the terms hereof. The execution, delivery and performance of this Agreement by Isis and the consummation by it of the transactions contemplated hereby (including the issuance of the Shares) have been duly authorized by Isis' Board of Directors (the ***"Board"***) and no further consent or authorization of Isis, the Board, or its stockholders is required. This Agreement has been duly executed by Isis and constitutes a legal, valid and binding obligation of Isis enforceable against Isis in accordance with its terms, except as enforceability may be limited by applicable bankruptcy, insolvency, reorganization, or moratorium or similar laws affecting creditors' and contracting parties' rights generally and except as enforceability may be subject to general principles of equity and except as rights to indemnity and contribution may be limited by state or federal securities laws or public policy underlying such laws.

2.3 Capitalization. The authorized capital stock of Isis, consists of 200,000,000 shares of Common Stock and 15,000,000 shares of Preferred Stock, of which 87,317,938 shares of Common Stock and no shares of Preferred Stock are issued and outstanding as of January 2, 2008. All of the issued and outstanding shares of Common Stock have been duly authorized, validly issued, fully paid, and nonassessable. Except as disclosed in the SEC Documents or issued pursuant to equity incentive plans identified in the SEC Documents, Isis does not have outstanding any options to purchase, or any preemptive rights or other rights to subscribe for or to purchase, any securities or obligations convertible into, or any contracts or commitments to issue or sell, shares of its capital stock or any such options, rights, convertible securities or obligations. Isis' Restated Certificate of Incorporation (the ***"Certificate of Incorporation"***), as in effect on the date hereof, and Isis' Bylaws (the ***"Bylaws"***) as in effect on the date hereof, are each filed as exhibits to the SEC Documents.

2.4 Issuance of Shares. The Shares are duly authorized and, upon issuance in accordance with the terms of this Agreement, will be validly issued, fully paid and non-assessable and will not be subject to preemptive rights or other similar rights of stockholders of Isis.

2.5 No Conflicts; Government Consents and Permits.

(a) The execution delivery and performance of this Agreement by Isis and the consummation by Isis of the transactions contemplated hereby (including the issuance of the Shares) will not (i) conflict with or result in a violation of any provision of Isis' Certificate of Incorporation or Bylaws, (ii) violate or conflict with, or result in a breach of any provision of, or constitute a default under, any agreement, indenture, or instrument to which Isis is a party, or (iii) result in a violation of any law, rule, regulation, order, judgment or decree (including United States federal and state securities laws and regulations and regulations of any self-regulatory organizations) applicable to Isis, except in the case of clauses (ii) and (iii) only, for such conflicts, breaches, defaults, and violations as would not reasonably be expected to have a

Material Adverse Effect or result in a liability for Genzyme. There is no control share acquisition, business combination, rights agreement or other anti-takeover provision contemplated by the Isis organizational documents or Delaware law that will become applicable to Genzyme as a result of the purchase of the Shares.

(b) Isis is not required to obtain any consent, authorization or order of, or make any filing or registration with, any court or governmental agency or any regulatory or self regulatory agency in order for it to execute, deliver or perform any of its obligations under this Agreement in accordance with the terms hereof, or to issue and sell the Shares in accordance with the terms hereof other than such as have been made or obtained, and except for (i) the registration of the Shares under the Securities Act pursuant to Section 6 hereof, (ii) any post-closing filings required to be made under federal or state securities laws, (iii) any required filings or notifications regarding the issuance or listing of additional shares with Nasdaq, and (iv) any consent required under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended (the ***"HSR Act"***).

(c) Isis has all franchises, permits, licenses, and any similar authority necessary for the conduct of its business as now being conducted by it and as currently proposed to be conducted as disclosed in the SEC Documents, except for such franchise, permit, license or similar authority, the lack of which would not reasonably be expected to have a Material Adverse Effect. Isis has not received any actual notice of any proceeding relating to revocation or modification of any such franchise, permit, license, or similar authority except where such revocation or modification would not reasonably be expected to have a Material Adverse Effect.

2.6 SEC Documents, Financial Statements. Isis has timely filed all reports, schedules, forms, statements and other documents required to be filed by it with the SEC for the three years prior to the date of this Agreement, pursuant to the reporting requirements of the Exchange Act (all of the foregoing filed at least two Business Days prior to the date hereof, including all exhibits included therein and financial statements and schedules thereto and documents (other than exhibits) incorporated by reference therein, being hereinafter referred to herein as the ***"SEC Documents"***). As of their respective dates, the SEC Documents complied in all material respects with the requirements of the Exchange Act and the rules and regulations of the SEC promulgated thereunder applicable to the SEC Documents, and none of the SEC Documents, at the time they were filed with the SEC, contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading. As of their respective dates, the Financial Statements and the related notes complied as to form and substance in all material respects with applicable accounting requirements and the published rules and regulations of the SEC with respect thereto. The Financial Statements and the related notes have been prepared in accordance with accounting principles generally accepted in the United States, consistently applied, during the periods involved (except (i) as may be otherwise indicated in the Financial Statements or the notes thereto, or (ii) in the case of unaudited interim statements, to the extent they may not include footnotes, may be condensed or summary statements or may conform to the SEC's rules and instructions for Reports on Form 10-Q) and fairly present in all material respects the consolidated financial position of Isis as of the dates thereof and the consolidated results of its operations and cash flows for the periods then ended (subject, in the case of unaudited statements, to normal and recurring year-end audit

adjustments). Neither Isis not any of its subsidiaries has any material liabilities of any nature, whether accrued, absolute, contingent or otherwise, other than liabilities adequately reflected or reserved against on the balance sheet dated September 30, 2007, included in the Form 10-Q filed by Isis for the quarter ended September 30, 2007, or incurred since September 30, 2007 in the ordinary course of business, consistent with past practice. All material agreements filed as exhibits to the SEC Documents under Item 601 of Regulation S-K (collectively, the ***"Material Agreements"***) are valid and enforceable against Isis in accordance with their respective terms, except for Material Agreements that have expired in accordance with their terms or as otherwise set forth in the SEC documents, and (i) as enforceability may be limited by applicable bankruptcy, insolvency, reorganization, or moratorium or similar laws affecting creditors' and contracting parties' rights generally, and (ii) as enforceability may be subject to general principles of equity and except as rights to indemnity and contribution may be limited by state or federal securities laws or public policy underlying such laws. Isis is not in breach of or default under any of the Material Agreements, and to Isis' knowledge, no other party to a Material Agreement is in breach of or default under such Material Agreement, except in each case, for such breaches or defaults as would not reasonably be expected to have a Material Adverse Effect. Isis has not received a notice of termination nor is Isis otherwise aware of any threats to terminate any of the Material Agreements. Since September 30, 2007, the business and operations of Isis and its subsidiaries have been conducted in the ordinary course consistent with past practice, and there have been and are no events or conditions that have resulted, or are reasonably expected to result, individually or collectively, in a Material Adverse Effect.

2.7 Investment Company. Isis is not and, after giving effect to the offering and sale of the Shares, will not be an "investment company" as such term is defined in the Investment Company Act of 1940, as amended (the ***"Investment Company Act"***). Isis will conduct its business in a manner so that it will not become subject to the Investment Company Act.

2.8 Nasdaq Global Market. The Common Stock is listed on Nasdaq, and, to Isis' knowledge, there are no proceedings to revoke or suspend such listing or the listing of the Shares. Isis is in compliance with the requirements of Nasdaq for continued listing of the Common Stock thereon and any other Nasdaq listing and maintenance requirements.

2.9 Private Placement. Neither Isis nor any person acting on its behalf, has, directly or indirectly, made any offers or sales of any security or solicited any offers to buy any security, under any circumstances that would require registration of the Shares under the Securities Act. Subject to the accuracy of the representations made by Genzyme in Section 3, the Shares will be issued and sold to Genzyme in compliance with applicable exemptions from the registration and prospectus delivery requirements of the Securities Act and the registration and qualification requirements of all applicable securities laws of the states of the United States. Isis has not engaged any brokers, finders or agents, or incurred, or will incur, directly or indirectly, any liability for brokerage or finder's fees or agents' commissions or any similar charges in connection with this Agreement and the transactions contemplated hereby.

SECTION 3. REPRESENTATIONS AND WARRANTIES OF GENZYME

Except as otherwise specifically contemplated by this Agreement, Genzyme hereby represents and warrants to Isis that:

3.1 Investment Purpose. Genzyme is purchasing the Shares for its own account and not with a present view toward the public distribution thereof and has no arrangement or understanding with any other persons regarding the distribution of such Shares except as would not result in a violation of the Securities Act. Genzyme will not, directly or indirectly, offer, sell, pledge, transfer or otherwise dispose of (or solicit any offers to buy, purchase or otherwise acquire or take a pledge of) any of the Shares except in accordance with the provisions of Section 6 or pursuant to and in accordance with the Securities Act.

3.2 Reliance on Exemptions. Genzyme understands that Isis intends for the Shares to be offered and sold to it in reliance upon specific exemptions from the registration requirements of United States federal and state securities laws and that Isis is relying upon the truth and accuracy of, and Genzyme's compliance with, the representations, warranties, agreements, acknowledgments and understandings of Genzyme set forth herein in order to determine the availability of such exemptions and the eligibility of Genzyme to acquire the Shares.

3.3 Accredited Investor; Access to Information. Genzyme is an "accredited investor" as defined in Regulation D under the Securities Act and is knowledgeable, sophisticated and experienced in making, and is qualified to make decisions with respect to investments in shares presenting an investment decision like that involved in the purchase of the Shares. Genzyme has been furnished with materials relating to the offer and sale of the Shares, that have been requested by Genzyme, including, without limitation, Isis' SEC Documents, and Genzyme has had the opportunity to review the SEC Documents. Genzyme has been afforded the opportunity to ask questions of Isis. Neither such inquiries nor any other investigation conducted by or on behalf of Genzyme or its representatives or counsel will modify, amend or affect Genzyme's right to rely on the truth, accuracy and completeness of the SEC Documents and Isis' representations and warranties contained in this Agreement. Genzyme has, with respect to all matters relating to this Agreement and the offer and sale of the Shares, not relied upon counsel to Isis except for the legal opinion to be delivered to Genzyme pursuant to Section 5.2(g).

3.4 Governmental Review. Genzyme understands that no United States federal or state agency or any other government or governmental agency has passed upon or made any recommendation or endorsement of the Shares or an investment therein.

3.5 Transfer or Resale. Genzyme understands that:

(a) the Shares have not been and are not being registered under the Securities Act (other than as contemplated in Section 6) or any applicable state securities laws and, consequently, Genzyme may have to bear the risk of owning the Shares for an indefinite period of time because the Shares may not be transferred unless (i) the resale of the Shares is registered pursuant to an effective registration statement under the Securities Act, as contemplated in Section 6; (ii) Genzyme has delivered to Isis an opinion of counsel (in form, substance and scope customary for opinions of counsel in comparable transactions) to the effect that the Shares to be sold or transferred may be sold or transferred pursuant to an exemption from such registration; or (iii) the Shares are sold or transferred pursuant to Rule 144;

(b) any sale of the Shares made in reliance on Rule 144 may be made only in accordance with the terms of Rule 144 and, if Rule 144 is not applicable, any resale of the Shares under circumstances in which the seller (or the person through whom the sale is made) may be deemed to be an

underwriter (as that term is defined in the Securities Act) may require compliance with some other exemption under the Securities Act or the rules and regulations of the SEC thereunder; and

(c) except as set forth in Section 6, neither Isis nor any other person is under any obligation to register the resale of the Shares under the Securities Act or any state securities laws or to comply with the terms and conditions of any exemption thereunder.

3.6 Legends. Genzyme understands the certificates representing the Shares will bear a restrictive legend in substantially the following form (and a stop-transfer order may be placed against transfer of the certificates for such Shares):

THE SECURITIES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, OR THE SECURITIES LAWS OF ANY STATE OF THE UNITED STATES. THE SECURITIES MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED, HYPOTHECATED, TRANSFERRED OR ASSIGNED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT FOR THE SECURITIES UNDER APPLICABLE SECURITIES LAWS, OR UNLESS OFFERED, SOLD, PLEDGED, HYPOTHECATED OR TRANSFERRED PURSUANT TO AN AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THOSE LAWS. ISIS PHARMACEUTICALS, INC., A DELAWARE CORPORATION ("ISIS") WILL BE ENTITLED TO REQUIRE AN OPINION OF COUNSEL SATISFACTORY TO ISIS THAT SUCH REGISTRATION IS NOT REQUIRED TO THE EXTENT THAT SUCH OPINION IS REQUIRED PURSUANT TO THAT CERTAIN STOCK PURCHASE AGREEMENT UNDER WHICH THE SECURITIES WERE ISSUED.

Genzyme may request that Isis remove, and Isis agrees to authorize and instruct (including by causing any required legal opinion to be provided) the removal of any legend from the Shares promptly (i) following any sale of the Shares pursuant to an effective Registration Statement or Rule 144, (ii) if the Shares are eligible for sale under Rule 144 without reference to volume or manner of sale limitations, or (iii) after the Registration Statement becomes effective. Any fees associated with the removal of the legend shall be borne by Isis; provided, however, Genzyme shall be responsible for fees incurred directly by Genzyme.

3.7 Authorization; Enforcement. Genzyme has the requisite corporate power and authority to enter into this Agreement and to consummate the transactions contemplated hereby. Genzyme has taken all necessary corporate action to authorize the execution, delivery and performance of this Agreement. Upon the execution and delivery of this Agreement, this Agreement will constitute a valid and binding obligation of Genzyme enforceable in accordance with its terms, except as enforceability may be limited by applicable bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' and contracting parties' rights generally and except as enforceability may be subject to general principles of equity and except as rights to indemnity and contribution may be limited by state or federal securities laws or public policy underlying such laws.

SECTION 4. COVENANTS OF THE PARTIES

4.1 Reporting Status. Isis' Common Stock is registered under Section 12 of the Exchange Act. During the Registration Period, Isis will timely file all documents required to be filed with the SEC, and Isis will not terminate its status as an issuer required to file reports under the Exchange Act even if the Exchange Act or the rules and regulations thereunder would permit such termination.

4.2 Expenses. Isis and Genzyme are each liable for, and will pay, their own expenses incurred in connection with the negotiation, preparation, execution and delivery of this Agreement, including, without limitation, attorneys' and consultants' fees and expenses.

4.3 Standstill and Holding Requirements. Genzyme agrees to comply with the restrictions and requirements set forth in Appendix 2.

SECTION 5. CONDITIONS TO CLOSING

5.1 Conditions to Obligations of Isis. Isis' obligation to complete the purchase and sale of the Shares and deliver such stock certificate(s) to Genzyme is subject to the fulfillment or waiver of the following conditions at or prior to the Closing:

(a) Receipt of Funds. Isis will have received immediately available funds in the full amount of the Purchase Price for the Shares being purchased hereunder.

(b) Representations and Warranties. The representations and warranties made by Genzyme in Section 3 will be true and correct in all material respects as of the Closing Date, except to the extent such representations and warranties are made as of another date, in which case such representations and warranties shall be true and correct in all material respects as of such other date.

(c) Covenants. All covenants, agreements and conditions contained in this Agreement to be performed by Genzyme on or prior to the Closing Date will have been performed or complied with in all material respects.

(d) Absence of Litigation. No proceeding challenging this Agreement or the transactions contemplated hereby, or seeking to prohibit, alter, prevent or materially delay the Closing, will have been instituted or be pending before any court, arbitrator, governmental body, agency or official.

(e) No Governmental Prohibition. The sale of the Shares by Isis will not be prohibited by the HSR Act, and will not be prohibited by any other law or governmental order or regulation.

5.2 Conditions to Purchase's Obligations at the Closing. Genzyme's obligation to complete the purchase and sale of the Shares is subject to the fulfillment or waiver of the following conditions at or before the Closing:

(a) Representations and Warranties. The representations and warranties made by Isis in Section 2 will be true and correct as of the Closing Date, except to the extent such representations and warranties are made as of another date, in which case such representations and warranties shall be

true and correct as of such other date.

(b) Covenants. All covenants, agreements and conditions contained in this Agreement to be performed by Isis on or prior to the Closing Date will have been performed or complied with in all material respects.

(c) Transfer Agent Instructions. Isis will have delivered to its transfer agent irrevocable written instructions to issue the Shares to Genzyme and deliver a certificate representing such Shares.

(d) Nasdaq Qualification. The Shares will be duly authorized for listing by Nasdaq, subject to official notice of issuance, to the extent required by the rules of Nasdaq.

(e) Absence of Litigation. No proceeding challenging this Agreement or the transactions contemplated hereby, or seeking to prohibit, alter, prevent or delay the Closing, will have been instituted or be pending before any court, arbitrator, governmental body, agency or official.

(f) No Governmental Prohibition. Any applicable waiting periods under the HSR Act shall have expired or terminated and any clearances, permits, authorizations, consents or approvals sought by Genzyme under any other applicable laws or regulations shall have been obtained. No statute, rule, regulation, executive order, decree, ruling, injunction, action, proceeding or interpretation shall have been enacted, entered, promulgated, endorsed or adopted by any court or governmental authority of competent jurisdiction or any self-regulatory organization or the staff of any of the foregoing, having authority over the matters contemplated hereby, which questions the validity of, or challenges or prohibits the consummation of, any of the transactions contemplated by this Agreement.

(g) Isis will have delivered to Genzyme a certificate signed by its Chief Executive Officer certifying that the conditions specified in the Section 5.2 with respect to Isis have been fulfilled. Isis shall have delivered to Genzyme (i) a copy of a certificate executed by the Secretary of Isis attaching and certifying to the truth and correctness of the Certificate of Incorporation, the Bylaws and the resolutions adopted by the Board in connection with the transactions contemplated by this Agreement, (ii) a good standing certificate dated as of a recent date, and (iii) an opinion from the general counsel of Isis regarding the matters in Sections 2.1, 2.2, the first sentence of 2.3, 2.4, 2.5, 2.7, and the second sentence of 2.9.

SECTION 6. REGISTRATION RIGHTS

6.1 As soon as reasonably practicable, but in no event later than 30 days after the Closing Date (the ***"Filing Date"***), Isis will file a registration statement covering the resale of the Registrable Securities on a registration statement (the ***"Registration Statement"***) with the SEC and effect the registration, qualifications or compliances (including, without limitation, the execution of any required undertaking to file post-effective amendments) as promptly as possible after the filing thereof, but in any event prior to the date (the ***"Effectiveness Date"***) which is (i)

90 days after the Closing Date if the Registration Statement is not reviewed by the SEC, or (ii) 120 days after the Closing Date, if the Registration Statement is reviewed by the SEC.

6.2 All Registration Expenses incurred in connection with any registration, qualification, exemption or compliance pursuant to Section 6.1 will be borne by Isis. All Selling Expenses relating to the sale of Registrable Securities by or on behalf of Genzyme will be borne by Genzyme.

6.3 In the case of the registration, qualification, exemption or compliance effected by Isis pursuant to this Agreement, Isis will, upon reasonable request, inform Genzyme as to the status of such registration, qualification, exemption and compliance. At its expense Isis will:

(a) except for such times as Isis is permitted hereunder to suspend the use of the prospectus forming part of the Registration Statement, use its commercially reasonable efforts to keep such registration, and any required qualification, exemption or compliance under state securities laws, continuously effective with respect to Genzyme and its permitted assignees, and to keep such Registration Statement free of any material misstatements or omissions, until the date all Shares held by Genzyme may be sold during any 90 day period under Rule 144 and any contractual agreements with Isis. The period of time during which Isis is required hereunder to keep the Registration Statement effective is referred to herein as the ***"Registration Period."***

(b) advise Genzyme promptly (and, in any event, within one Business Day):

(i) when the Registration Statement or any amendment thereto has been filed with the SEC and when the Registration Statement or any post-effective amendment thereto has become effective;

(ii) of the receipt by Isis of any notification from the SEC of any stop order suspending the effectiveness of the Registration Statement or the initiation of any proceedings for such purpose;

(iii) of the receipt by Isis of any notification with respect to the suspension of the qualification of the Registrable Securities included therein for sale in any jurisdiction or the initiation or threatening of any proceeding for such purpose; and

(iv) of the occurrence of any event that requires the making of any changes in the Registration Statement or the prospectus so that, as of such date, the statements therein are not misleading and do not omit to state a material fact required to be stated therein or necessary to make the statements therein (in the case of the prospectus, in the light of the circumstances under which they were made) not misleading;

(c) use its commercially reasonable efforts to obtain the withdrawal of any order suspending the effectiveness of any Registration Statement as soon as reasonably practicable;

(d) if Genzyme so requests in writing, promptly furnish to Genzyme, without charge, at least one copy of such Registration Statement and any post-effective amendment

thereto, including financial statements and schedules, and, if explicitly requested, all exhibits in the form filed with the SEC;

(e) during the Registration Period, promptly deliver to Genzyme, without charge, at least one copy of the prospectus included in such Registration Statement and any amendment or supplement thereto and as many additional copies as Genzyme may reasonably request; and Isis consents to the use, consistent with the provisions hereof, of the prospectus or any amendment or supplement thereto by Genzyme in connection with the offering and sale of the Registrable Securities covered by the prospectus or any amendment or supplement thereto;

(f) during the Registration Period, if Genzyme so requests in writing, deliver to Genzyme, without charge, (i) one copy of the following documents, other than those documents available via EDGAR (and excluding, in each case, exhibits thereto): (A) its annual report to its stockholders, if any (which annual report will contain financial statements audited in accordance with generally accepted accounting principles in the United States of America by a firm of certified public accountants of recognized standing), (B) if not included in substance in its annual report to stockholders, its annual report on Form 10-K (or similar form), (C) its definitive proxy statement with respect to its annual meeting of stockholders, (D) each of its quarterly reports to its stockholders, and, if not included in substance in its quarterly reports to stockholders, its quarterly report on Form 10-Q (or similar form), and (E) a copy of the Registration Statement; and (ii) if explicitly requested, any exhibits filed with respect to the foregoing;

(g) upon the occurrence of any event contemplated by Section 6.3(b)(v) above, except for such times as Isis is permitted hereunder to suspend the use of the prospectus forming part of the Registration Statement, Isis will use its commercially reasonable efforts to as soon as reasonably practicable prepare a post-effective amendment to the Registration Statement or a supplement to the related prospectus, or file any other required document so that, as thereafter delivered to Genzyme, the prospectus will not include any untrue statement of a material fact or omit to state any material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading;

(h) otherwise use its commercially reasonable efforts to comply in all material respects with all applicable rules and regulations of the SEC which could affect the sale of the Registrable Securities;

(i) use its commercially reasonable efforts to cause all Registrable Securities to be listed on each securities exchange or market, if any, on which equity securities issued by Isis have been listed;

(j) use its commercially reasonable efforts to take all other steps necessary to effect the registration of the Registrable Securities contemplated hereby and to enable Genzyme to sell Registrable Securities under Rule 144; and

(k) permit a single counsel for Genzyme to review the Registration Statement and all amendments and supplements thereto, within two Business Days prior to the filing thereof with the Commission;

provided that, in the case of clause (k) above, Isis will not be required to delay the filing of the Registration Statement or any amendment or supplement thereto to incorporate any comments to the Registration Statement or any amendment or supplement thereto by or on behalf of Genzyme if such comments would require a delay in the filing of such Registration Statement, amendment or supplement, as the case may be.

If at any time during the Registration Period there is not an effective Registration Statement covering all of the Registrable Securities and Isis shall determine to prepare and file with the SEC a registration statement relating to an offering for its own account or the account of others under the Securities Act of any of its equity securities, other than on Form S-4 or Form S-8 (each as promulgated under the Securities Act) or their then equivalents relating to equity securities to be issued solely in connection with any acquisition of a business or equity securities issuable in connection with stock option or other employee or director benefit plans, then Isis shall send to Genzyme written notice of such determination and, if within ten Business Days after receipt of such notice, Genzyme shall so request in writing, Isis shall include in such registration statement all or any part of such Registrable Securities Genzyme requests to be registered, subject to customary underwriter cutbacks applicable to all holders of registration rights on a pro rata basis (along with other holders of piggyback registration rights with respect to Isis); provided, that (i) if at any time after giving written notice of its intention to register any securities and prior to the effective date of the registration statement filed in connection with such registration, Isis shall determine for any reason not to register or to delay registration of such securities, Isis may, at its election, give written notice of such determination to Genzyme and, thereupon, (A) in the case of a determination not to register, shall be relieved of its obligation to register any Registrable Securities to this paragraph in connection with such registration (but not from its obligation to pay expenses in accordance with this Agreement, and (B) in the case of a determination to delay registering, shall be permitted to delay registering any Registrable Securities being registered pursuant to this paragraph for the same period as the delay in registering such other securities and (ii) if such registration involves an underwritten public offering, a condition to having any Registrable Securities included in such registration shall be Genzyme or its permitted assignees entering into an underwriting agreement in customary form and agreeing to sell such Registrable Securities to the underwriters on the same terms and conditions as Isis (provided, however, that in no event shall Genzyme or any permitted transferee be required to provide any indemnification or contribution in favor of any underwriters on terms more favorable than the terms set forth in this Agreement).

6.4 Genzyme will have no right to take any action to restrain, enjoin or otherwise delay any registration pursuant to Section 6.1 hereof as a result of any controversy that may arise with respect to the interpretation or implementation of this Agreement.

6.5 **(a)** To the extent permitted by law, Isis will indemnify and hold harmless Genzyme, each Genzyme director and officer and each person controlling Genzyme within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act, with respect to which any registration that has been effected pursuant to this Agreement, against all claims, losses, damages, penalties, fines, charges and liabilities (or action in respect thereof), including any of the foregoing incurred in settlement of any litigation, commenced or threatened (subject to Section 6.5(c) below), arising out of or based on any untrue statement (or alleged untrue statement) of a material fact contained in the Registration Statement, prospectus, any amendment

or supplement thereof, or other document incident to any such registration, qualification or compliance or based on any omission (or alleged omission) to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, in light of the circumstances in which they were made, and will reimburse Genzyme and each director, officer and person controlling Genzyme, for reasonable legal and other out-of-pocket expenses incurred in connection with investigating or defending any such claim, loss, damage, liability or action as incurred; provided that Isis will not be liable in any such case to the extent that any untrue statement or omission or allegation thereof is made in reliance upon and in conformity with written information furnished to Isis by or on behalf of Genzyme specifically for use in such Registration Statement, prospectus, amendment or supplement; *provided further* that Isis will not be liable in any such case where the claim, loss, damage or liability arises solely out of the failure of Genzyme to comply with Section 6.6 of this Agreement respecting sales of Registrable Securities, and except that the foregoing indemnity agreement is subject to the condition that, insofar as it relates to any such untrue statement or alleged untrue statement or omission or alleged omission made in the preliminary prospectus but eliminated in the amended prospectus on file with the SEC at the time the Registration Statement becomes effective or in the amended prospectus filed with the SEC pursuant to Rule 424(b) of the Securities Act, which meets the requirements of Section 10(a) of the Securities Act (the ***"Final Prospectus"***), such indemnity will not inure to the benefit of Genzyme or any such controlling person, if a copy of the Final Prospectus had been furnished by Isis to Genzyme for delivery was not furnished to the person or entity asserting the loss, liability, claim or damage prior to the time such furnishing was required by the Securities Act and the Final Prospectus would have cured all defects giving rise to such loss, liability, claim or damage.

(b) Genzyme will severally, and not jointly, indemnify Isis, each of its directors and officers, and each person who controls Isis within the meaning of Section 15 of the Securities Act, against all claims, losses, damages and liabilities (or actions in respect thereof), including any of the foregoing incurred in settlement of any litigation, commenced or threatened (subject to Section 6.5(c) below), to the extent arising out of or based on any untrue statement of a material fact contained in the Registration Statement, prospectus, or any amendment or supplement thereof, incident to any such registration, or based on any omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, in light of the circumstances in which they were made, and will reimburse Isis, such directors and officers, and each person controlling Isis for reasonable legal and any other expenses reasonably incurred in connection with investigating or defending any such claim, loss, damage, liability or action as incurred, in each case to the extent, but only to the extent, that such untrue statement or omission or allegation thereof is made in reliance upon and in conformity with written information furnished to Isis by or on behalf of Genzyme specifically for use in the Registration Statement, prospectus, amendment or supplement. Notwithstanding the foregoing, Genzyme's aggregate liability pursuant to this subsection (b) and subsection (d) will be limited to the net amount received by Genzyme from the sale of the Registrable Securities.

(c) Each party entitled to indemnification under this Section 6.5 (the ***"Indemnified Party"***) will give notice to the party required to provide indemnification (the ***"Indemnifying Party"***) promptly after such Indemnified Party has actual knowledge of any claim as to which indemnity may be sought, and will permit the Indemnifying Party (at its expense) to assume the defense of any such claim or any litigation resulting therefrom, provided

that counsel for the Indemnifying Party, who will conduct the defense of such claim or litigation, will be approved by the Indemnified Party (whose approval will not unreasonably be withheld), and the Indemnified Party may participate in such defense at such Indemnified Party's expense, and provided further that the failure of any Indemnified Party to give notice as provided herein will not relieve the Indemnifying Party of its obligations under this Agreement, except to the extent such failure is materially prejudicial to the Indemnifying Party in defending such claim or litigation, provided, however, that the Indemnified Parties shall each have the right to retain their own counsel with the fees and expenses of not more than one counsel for the Indemnified Parties as a group to be paid by the indemnifying party, if, in the reasonable opinion of counsel retained by an Indemnified Party, the representation by separate counsel of all the Indemnified Parties and the indemnifying party would be inappropriate due to actual or potential conflicting interests between any Indemnified Party and any other party represented by such counsel in such proceeding. An Indemnifying Party will not be liable for any settlement of an action or claim effected without its written consent (which consent will not be unreasonably withheld). No Indemnifying Party, in its defense of any such claim or litigation, will, except with the consent of each Indemnified Party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation. The indemnifying party shall keep each Indemnified Party apprised as to the status of the defense or any settlement negotiations with respect thereto. No indemnifying party shall, without the prior written consent of an Indemnified Party, consent to entry of any judgment or enter into any settlement or other compromise which requires any admission of wrongdoing by such Indemnified Party or obligates or requires an Indemnified Party to take, or refrain from taking, any action.

(d) If the indemnification provided for in this Section 6.5 is held by a court of competent jurisdiction to be unavailable to an Indemnified Party with respect to any loss, liability, claim, damage or expense referred to therein, then the Indemnifying Party, in lieu of indemnifying such Indemnified Party thereunder, will contribute to the amount paid or payable by such Indemnified Party as a result of such loss, liability, claim, damage or expense in such proportion as is appropriate to reflect the relative fault of the Indemnifying Party on the one hand and of the Indemnified Party on the other in connection with the statements or omissions which resulted in such loss, liability, claim, damage or expense as well as any other relevant equitable considerations. The relative fault of the Indemnifying Party and of the Indemnified Party will be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission to state a material fact relates to information supplied by the Indemnifying Party or by the Indemnified Party and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

6.6 **(a)** Genzyme agrees that, within one Business Day following receipt of any written notice from Isis specifically stating that there has occurred the happening of an event requiring the preparation of a supplement or amendment to a prospectus relating to Registrable Securities so that, as thereafter delivered to Genzyme, such prospectus will not contain an untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading, Genzyme will discontinue disposition of Registrable Securities pursuant to the Registration Statement and prospectus contemplated by Section 6.1 until its receipt of copies of the supplemented or amended prospectus from Isis and,

if so directed in writing by Isis, Genzyme will deliver to Isis or destroy all copies, other than permanent file copies then in Genzyme's possession, of the prospectus covering such Registrable Securities at the time of receipt of such notice.

(b) Genzyme will be obligated to suspend, upon request of Isis pursuant to Section 6.6(a), any disposition of Registrable Securities pursuant to the Registration Statement and prospectus contemplated by Section 6.1 during no more than two periods of no more than 30 calendar days each

during any 12-month period and only to the extent that Genzyme has received notice from Isis specifically stating that the Board has determined in good faith that the sale of Registrable Securities under the Registration Statement would be reasonably likely to cause a violation of the Securities Act or Exchange Act.

(c) As a condition to the inclusion of its Registrable Securities, Genzyme will furnish to Isis such information regarding Genzyme and the distribution proposed by Genzyme as Isis may reasonably request in writing, including completing a Registration Statement questionnaire in customary form.

(d) Genzyme hereby covenants with Isis (i) not to make any sale of the Registrable Securities without effectively causing any applicable prospectus delivery requirements under the Securities Act to be satisfied, and (ii) if such Registrable Securities are to be sold by any method or in any transaction other than on a national securities exchange, Nasdaq or in the over-the-counter market, in privately negotiated transactions, or in a combination of such methods, to notify Isis at least five Business Days prior to the date on which Genzyme first offers to sell any such Registrable Securities.

(e) [Intentionally omitted]

(f) Genzyme agrees not to take any action with respect to any distribution deemed to be made pursuant to such Registration Statement which would constitute a violation of Regulation M under the Exchange Act or any other applicable rule, regulation or law.

(g) At the end of the Registration Period Genzyme will discontinue sales of shares pursuant to such Registration Statement upon receipt of notice from Isis of its intention to remove from registration the shares covered by such Registration Statement which remain unsold, and Genzyme will notify Isis of the number of shares registered which remain unsold within five Business Days after receipt of such notice from Isis.

6.7 The rights of Genzyme under any provision of this Section 6 may be waived (either generally or in a particular instance, either retroactively or prospectively and either for a specified period of time or indefinitely) or amended by an instrument in writing signed by Genzyme.

SECTION 7. GOVERNING LAW; MISCELLANEOUS.

7.1 Governing Law; Jurisdiction. This Agreement will be governed by and interpreted in accordance with the laws of the State of Delaware without regard to the principles of conflict of laws.

7.2 Counterparts; Signatures by Facsimile. This Agreement may be executed in two counterparts, both of which are considered one and the same agreement and will become effective when the counterparts have been signed by each party and delivered to the other party hereto. This Agreement, once executed by a party, may be delivered to the other party hereto by facsimile transmission of a copy of this Agreement bearing the signature of the party so delivering this Agreement.

7.3 Headings. The headings of this Agreement are for convenience of reference only, are not part of this Agreement and do not affect its interpretation.

7.4 Severability. If any provision of this Agreement is invalid or unenforceable under any applicable statute or rule of law, then such provision will be deemed modified in order to conform with such statute or rule of law. Any provision hereof that may prove invalid or unenforceable under any law will not affect the validity or enforceability of any other provision hereof.

7.5 Entire Agreement; Amendments. This Agreement (including any schedules and exhibits hereto) and the License and Research Agreement constitute the entire agreement among the parties hereto with respect to the subject matter hereof and thereof. There are no restrictions, promises, warranties or undertakings, other than those set forth or referred to herein or therein. This Agreement supersedes all prior agreements and understandings among the parties hereto with respect to the subject matter hereof. No provision of this Agreement may be waived or amended other than by an instrument in writing signed by the party to be charged with enforcement. Any amendment or waiver effected in accordance with this Section 7.5 will be binding upon Genzyme and Isis.

7.6 Notices. All notices required or permitted hereunder will be in writing and will be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed email or facsimile if sent during normal business hours of the recipient, if not, then on the next Business Day, or (c) one Business Day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. The addresses for such communications are:

If to Isis:	Isis Pharmaceuticals 1896 Rutherford Road Carlsbad, CA 92008 Attn: COO Facsimile: 760-603-2700
With a copy to:	ISIS GENERAL COUNSEL Facsimile: 760-268-4922
If to Genzyme:	Genzyme Corporation 500 Kendall Street Cambridge, MA 02142 Attn: General Counsel Facsimile: 617-252-7600

7.7 Successors and Assigns. This Agreement is binding upon and inures to the benefit of the parties and their successors and assigns. Isis will not assign this Agreement or any rights or obligations hereunder without the prior written consent of Genzyme, and Genzyme will not assign this Agreement or any rights or obligations hereunder without the prior written consent of Isis; provided, however, that Genzyme may assign this Agreement together with all of the Shares it then owns (in accordance with the terms of Sections 3.5 and 3.6) to any wholly-owned subsidiary and any such assignee may assign the Agreement together with all of the Shares it then owns (in accordance with the terms of Sections 3.5 and 3.6) to Genzyme or any other subsidiary wholly-owned by Genzyme, in any such case, without such consent provided that the assignee agrees to assume Genzyme's obligations under Appendix 2 of this Agreement.

7.8 Third Party Beneficiaries. This Agreement is intended for the benefit of the parties hereto, their respective permitted successors and assigns, and is not for the benefit of, nor may any provision hereof be enforced by, any other person.

7.9 Further Assurances. Each party will do and perform, or cause to be done and performed, all such further acts and things, and will execute and deliver all other agreements, certificates, instruments and documents, as the other party may reasonably request in order to carry out the intent and accomplish the purposes of this Agreement and the consummation of the transactions contemplated hereby.

7.10 No Strict Construction. The language used in this Agreement is deemed to be the language chosen by the parties to express their mutual intent, and no rules of strict construction will be applied against a party.

7.11 Equitable Relief. Isis recognizes that, if it fails to perform or discharge any of its obligations under this Agreement, any remedy at law may prove to be inadequate relief to Genzyme. Isis therefore agrees that Genzyme are entitled to seek temporary and permanent injunctive relief in any such case. Genzyme also recognizes that, if it fails to perform or discharge any of its obligations under this Agreement, any remedy at law may prove to be

inadequate relief to Isis. Genzyme therefore agrees that Isis is entitled to seek temporary and permanent injunctive relief in any such case.

7.12 Survival of Representations and Warranties. Notwithstanding any investigation made by a party to this Agreement, all representations and warranties made by Isis and Genzyme herein will survive for a period of one year following the date hereof.

IN WITNESS WHEREOF, Genzyme and Isis have caused this Stock Purchase Agreement to be duly executed as of the date first above written.

GENZYME CORPORATION

By: /s/ Earl M. Collier, Jr.

Its: EVP

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall

Its: COO & CFO

APPENDIX 1

DEFINED TERMS

"Business Day" means a day Monday through Friday on which banks are generally open for business in the State of California.

"Exchange Act" means the Securities Exchange Act of 1934, as amended.

"Financial Statements" means the financial statements of Isis included in the SEC Documents.

"Material Adverse Effect" means a material adverse effect on (a) the business, operations, assets or financial condition of Isis, taken as a whole, or (b) the ability of Isis to perform its obligations pursuant to the transactions contemplated by this Agreement.

"Nasdaq" means The Nasdaq Global Market.

"Person" means any person, individual, corporation, limited liability company, partnership, trust or other nongovernmental entity or any governmental agency, court, authority or other body (whether foreign, federal, state, local or otherwise).

The terms ***"register," "registered"*** and ***"registration"*** refer to the registration effected by preparing and filing a registration statement in compliance with the Securities Act, and the declaration or ordering of the effectiveness of such registration statement.

"Registrable Securities" means the Shares; *provided*, *however*, that securities will only be treated as Registrable Securities if and only for so long as they (A) have not been disposed of pursuant to a registration statement declared effective by the SEC and (B) have not been sold in a transaction exempt from the registration and prospectus delivery requirements of the Securities Act so that all transfer restrictions and restrictive legends with respect thereto are removed upon the consummation of such sale.

"Registration Expenses" means all expenses incurred by Isis in complying with Section 6.1 hereof, including, without limitation, all registration, qualification and filing fees, printing expenses, escrow fees, fees and expenses of counsel for Isis (but excluding the Selling Expenses).

"Rule 144" means Rule 144 promulgated under the Securities Act, or any successor rule.

"SEC" means the United States Securities and Exchange Commission.

"Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations thereunder, or any similar successor statute.

"Selling Expenses" means all selling commissions applicable to the sale of Registrable Securities and all fees and expenses of legal counsel for Genzyme.

"Trading Market" means Nasdaq or any national securities exchange, market or trading or quotation facility on which the Common Stock is then listed or quoted.

APPENDIX 2

STANDSTILL AND HOLDING REQUIREMENTS

1. Restrictions. Prior to the earlier of (a) the ten-year anniversary of the effective date of the License and Research Agreement or (b) the date on which Genzyme holds less than 2% of Isis' outstanding Common Stock on an issued and outstanding basis without giving effect to any convertible securities, except as contemplated by this Stock Purchase Agreement, Genzyme and its Affiliates will not, directly or indirectly:

(i) acquire, agree to acquire, or publicly offer to acquire beneficial ownership (within the meaning of Rule 13d-3 under the Exchange Act) of any Isis voting securities;

(ii) participate in any "solicitation" of "proxies" to vote (as such terms are used in the proxy rules of the SEC promulgated pursuant to Section 14 of the Exchange Act) with respect to any Isis voting securities;

(iii) form, join or in any way participate in a "group" within the meaning of Section 13(d)(3) of the Exchange Act with respect to any Isis voting securities;

(iv) publicly propose any business combination, restructuring, recapitalization or similar transaction involving Isis or any of its subsidiaries; nominate any person as a director of Isis who is not nominated by the then incumbent directors or a committee thereof; or propose any matter to be voted upon by the stockholders of Isis that relates to a business combination, restructuring, recapitalization or similar transaction involving Isis;

(v) bring any legal action contesting or otherwise challenge in a legal proceeding the validity of this Section 1 of Appendix 2; or

(vi) enter into any agreement with a third party to do any of the actions prohibited under (i), (ii), (iii) (iv) or (v) above.

2. Termination of Limitations. The limitations provided in Section 1 of this Appendix 2 will terminate:

(a) following the commencement by any Third Party of a tender or exchange offer seeking to acquire beneficial ownership of fifty percent (50%) or more of the outstanding shares of Isis Common Stock;

(b) following the public announcement of the execution of an agreement which, if consummated, would result in either (i) the beneficial owners of Isis Common Stock beforehand owning less than 50% of the voting securities or voting power of the surviving company in the transaction or (ii) the sale of all or substantially all of the assets of Isis;

(c) upon the filing of a preliminary or final proxy statement by any Third Party with respect to the commencement of a proxy or consent solicitation subject to Section 14 of the Exchange Act to elect or remove a majority of the directors of Isis;

(d) upon the adoption of a plan of liquidation or dissolution with respect to Isis; or

(e) upon written consent from Isis.

3. Agreement to Hold Shares. Genzyme agrees that it will hold and will not sell the Shares (or otherwise make any short sale of, grant any option for the purchase of, or enter into any hedging or similar transaction with the same economic effect as a sale of the Shares) until the earlier of (a) the 4-year anniversary of the effective date of the License and Research Agreement, (b) the first commercial sale of a Product under the License and Research

Agreement or (c) termination or reversion of the product license granted to Genzyme under the License and Research Agreement (the "Holding Period"). In addition, after the expiration of the Holding Period, Genzyme will not sell more than 500,000 Shares in any thirty (30) day period.

4. Affiliate. For the purposes of this Appendix 2, "Affiliate" of an entity means any other entity that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such first entity. For purposes of this definition only, "control" (and, with correlative meanings, the terms "controlled by" and "under common control with") means the possession of the actual power to direct the management or policies of an entity, whether through the ownership of voting securities or by contract relating to voting rights or corporate governance. In addition, Regulus Therapeutics, LLC will not be considered an Affiliate of Isis.

Exhibit B

Product Term Sheet

EXHIBIT B

Collaboration and License Agreement
Isis Pharmaceuticals and Genzyme
Product Term Sheet

January 7, 2008

Capitalized terms used but not defined in this Product Term Sheet are used with the meanings given to them in the License and Research Agreement.

Scope: Genzyme will exclusively license the apoB program, for therapeutic purposes. Genzyme will be responsible for the continued development and commercialization of the Product, subject to profit sharing and milestone payments paid to Isis.

Isis Grants: As described in License and Research Agreement.

Product As described in License and Research Agreement.

Restrictions on Cross Use of Product and Non-Competition: As described in License and Research Agreement.

Cross-License Genzyme will grant Isis a first option to negotiate a license to practice any technology Genzyme discovers or develops as part of its program to develop or commercialize the Product that would be relevant to antisense therapeutics as a whole, including but not limited to manufacturing, formulation and delivery technologies, with appropriate consideration to be negotiated in good faith by the parties.

License Fee and Up-Front Payments: Genzyme will pay to Isis an up-front, non-refundable, non-creditable license fee in the amount of US $175M payable as described in the License and Research Agreement.

Milestones: Genzyme will pay Isis the following cash payments for the achievement of the following milestones of the Product by Genzyme or a sublicensee.

Mipomersen in familial hypercholesterolemia (FH):

Event	Milestone
U.S. NDA Filing	US$ [***]
U.S. NDA Approval HoFH	US$ [***]
U.S. NDA Approval HeFH	US$ [***]
MAA Approval for FH	US$ [***]

Mipomersen in first non-FH indication:

Event	Milestone
U.S. NDA Approval	US$ [***]
MAA Approval	US$ [***]
JNDA Approval	US$ [***]

Follow-On Product:

Event	Milestone
Aggregate Milestones	US$ [***]

The parties will mutually agree on development and regulatory strategy and allocation of milestones based on various regulatory approvals.

Sales milestones for annual sales of Products

Event (must reach level for two consecutive years)	Milestone
Achievement of US$ 3B in total annual sales	US$ [***]
Achievement of US$ 4B in total annual sales	US$ [***]
Achievement of US$ 5B in total annual sales	US$ [***]

Sales milestones are achieved one time only, regardless of Product.

Development and Commercialization Roles and Responsibilities:

Development Plan:

As part of the More Detailed Product Agreement, the parties will agree to a Development Plan for the Product. The Development Plan will include a detailed budget of development costs and will be managed by a Joint Development Committee ("JDC") comprised of equal members from both Parties for the initial [***] years following the Effective Date [***]. The JDC will act by unanimous consent, with each party having a single vote. Disputes that cannot be resolved by the JDC will be referred initially to designated senior officers of Isis and Genzyme and then, if necessary, to mediation.

Roles and Responsibilities:

- Isis will transfer to Genzyme all requested preclinical pharmacology and safety data, clinical data, and other information related to the Product.
- Attachment B sets forth Isis' recommendations regarding which trials in 2008 Isis will conduct, which trials Genzyme will conduct, and which trials Isis will transition to Genzyme over the first half of the year pursuant to a mutually agreed upon plan.
- Except as otherwise determined by the JDC, Genzyme will conduct all clinical trials and all preclinical work initiated in 2009 and thereafter, and will be responsible for worldwide regulatory support for the Product including NDA preparation and submission.
- Isis will fund the studies described as Isis-funded in Attachment B plus the first $75 million of the remaining external development expense for the Product (calculated beginning January 1, 2008) including, without limitation, clinical trial expense for the remaining studies in Attachment B (non Isis-funded) and future studies, toxicology (except for Isis-funded studies) and PK studies, API and drug product, (including packaging and distribution), SAB and DSMB expense, etc. Beginning when the initial $75 million in external development expense has been funded by Isis, all development costs (internal and external) except the costs for the studies described as Isis funded in Attachment B if such studies are still ongoing will be treated as Program Costs.
- Genzyme will be responsible for all of Genzyme's internal labor costs and for all Program Costs after the first $75 million of external expenditure funded by Isis until the Program achieves profitability (provided, however, that before the Program achieves profitability, Isis internal labor will not be reimbursed by Genzyme).
- Except for the specific tasks assigned to Isis above, Genzyme (subject to JDC oversight) shall be responsible for all other aspects of the development and commercialization of the Product, the costs for which, except as otherwise described above, shall be deemed to be Program Costs.
- Genzyme will provide to Isis, at Isis' request, any and all data from clinical or preclinical studies with Product(s).

"Program Costs" means all costs and expenses incurred by Genzyme or Isis in connection with the commercial manufacture, promotion and sale of the Product, including all royalties, milestones and license fees payable to third-parties (including those currently owed to [***] and [***]), the costs of all clinical trials and preclinical studies, the costs to produce and maintain a CMC document to support product manufacturing including, without limitation, stability studies, and other validation activities, and costs associated with obtaining and maintaining regulatory approvals for the Product. Program Costs specifically will not include the purchase price for the Shares, the license fee or milestones payable to Isis. Program Costs will also not include the costs to prosecute and maintain Patents which will be dealt with as described later in this term sheet. The Parties will agree on a chart of accounts to determine Program Costs relying in general on the principles attached as Attachment A.

Profit Sharing

In lieu of royalties on Product sales, the Parties will share the profits from sales of all Product beginning in any year in which such Product generates Net Profits. The Parties will then divide Net Profits pursuant to an allocation as follows:

For Annual Net Revenues	Genzyme Profit %
$1 - ≤$200 M	70%
[***]	
>$2 B	50%

In any year in which Program Costs for such year exceed Net Revenue for such year, Genzyme's share of Net Revenue will be 100% and Genzyme will be solely responsible for all Program Costs.

Notwithstanding the foregoing, in any year in which Net Profits are generated in an amount greater than or equal to [***] of Net Revenue, Isis' share of Net Profits shall not fall below an amount equal to [***] of Net Revenue.

For the purposes of this Term Sheet, "Net Profit" for any calendar year in which Net Revenue exceeds Program

Costs is defined as all Net Revenue derived from sales or license of Product in such year, minus all Program Costs borne by the parties during such year (which, for items that need to be mutually agreed to, are within a mutually agreed budget). "Net Revenue" means the gross invoiced sales amount of Product billed by Genzyme and its affiliates for the sale of Product during the applicable year, minus standard deductions taken in accordance with standard allocation procedures and accounting methods or any revenue received by Genzyme in connection with the license of a Product or grant of any other rights to a product such as distribution rights.

Licensed Patents: The Licensed Patents are defined in the License and Research Agreement.

Following the signing of the More Detailed Product Agreement, Isis will assign the Product-Specific Patents to Genzyme, and Genzyme will be responsible at its own expense for prosecuting and maintaining such patents and any future Product-Specific Patents. Isis will be responsible for all costs of prosecuting and maintaining Isis Core Technology Patents and the Isis Manufacturing and Analytical Patents. Even though [***] is a Product-Specific Patent, Isis will not assign such [***] to Genzyme, but Genzyme will have the first right to prosecute, maintain and enforce the [***] at Genzyme's expense.

Joint Patent Review Meetings.

At least once a quarter, Isis and Genzyme patent professionals will meet to discuss prosecution strategy for the Licensed Patents in so far as relevant to maintaining the broadest coverage for the Products.

The patent professionals will also discuss any potential third party infringement of patents that might affect the Products, and any third party licenses that might be necessary or useful to maximize the value of the Products. The expenses associated with any licensing or action to pursue an infringer that is mutually agreed between the Parties will be included in Program Costs. Similarly, any recoveries made by a Party in enforcing a Licensed Patent that is mutually agreed to be enforced will be included in Net Revenues.

Research Support The parties will agree on a research program that may include, but is not limited to, the following research topics; [***]

Isis will fund research expenses, for these programs in [***]. Genzyme will fund the research expenses, for these programs in [***], and the cost of such research programs will not be included in Program Costs.

The nature and scope of this research program will be determined by JDC.

[***] Technology: Without first obtaining Genzyme's written consent (such consent not to be unreasonably withheld), Isis will not license to a Third Party any technology that (i) is specifically useful in [***], but is not broadly applicable to other [***], and (ii) was invented by Isis while performing the research or development plan funded by Genzyme under the Product License.

Safety Database: Isis maintains a database that includes information regarding the tolerability of its drug compounds, individually and as a class, including information discovered during pre-clinical and clinical development (the "Isis Database"). In an effort to maximize understanding of the safety profile and pharmacokinetics of Isis compounds, Genzyme will cooperate in connection with populating the Isis Database. In accordance with Applicable Law and any applicable informed consents or other Third Party obligations, Genzyme will provide Isis with copies of toxicology, pharmacokinetic and serious adverse event final reports related to each Product plus any supporting data reasonably requested by Isis.

Term: The term of the Product License will be perpetual subject to termination and reversion rights.

Reversion Rights: Should Genzyme not advance the Product using commercially reasonable efforts or discontinue development or commercialization of the Product, then all rights to the Product will revert back to Isis (the "Reversion"), including a license to or reassignment of all patent claims and transfer of all data and regulatory filings controlled by Genzyme that are necessary to develop and commercialize the Product solely for such purpose. The license will be sublicensable.

Notwithstanding the foregoing, in the event that the approved label for the Product [***] that are not currently anticipated by the parties, the parties will discuss in good faith the extent to which such [***] changes the [***] for the Product.

In consideration for the Reversion, Genzyme would receive a royalty on Net Revenue. Genzyme's royalty would be (i) [***] of Net Revenue if the Reversion occurred prior to the approval of the Product in an FH indication, (ii) [***] of Net Revenue if the Reversion occurred prior to the approval of the Product for a non-FH indication, and (iii) [***] of Net Revenue if the Reversion occurred at the time of or after the approval of the Product for a non-FH indication. Notwithstanding the foregoing in no event will the total royalty payable to Genzyme exceed the aggregate amount of Program Costs that Genzyme has contributed to the Product, with interest thereon at [***] per year, net of any amounts paid for by Isis or covered by Product Revenue.

Manufacture of Product	Isis will supply the API for the Product for the Phase 2 clinical trials at the cost that Isis calculates on an annual basis as its fully-burdened cost. Further, Isis agrees to supply the Pivotal Trial and initial launch supply of API for the Product at its fully burdened cost, as calculate on an annual basis, which costs will be included in Program Costs and the calculation of Net Profit. The parties will enter into a supply agreement for Isis' supply of the API for the Product which will contain mutually agreeable terms and conditions. The Parties anticipate that Genzyme will build manufacturing capability to manufacture API for commercial supply, however, Genzyme and Isis will mutually agree on the use of third parties to manufacture the Product.
Indemnity	Each Party will indemnify the other Party, from and against any third party claims to the extent occurring as a result of the negligence or willful misconduct of the indemnifying party; except to the extent such claims result from the gross negligence or willful misconduct of any party seeking indemnification.
Change of Control	In the event of a Change of Control of Isis, Genzyme shall have the right to (i) purchase Isis' interest in the Product at the then-applicable fair market value (as determined by a mutually agreeable third party) and/or (ii) terminate (a) the participation of the successor to Isis in any ongoing research and development programs and Genzyme's funding obligations associated therewith, and (b) the right of the successor to Isis to sit on the JDC or otherwise exercise any control over the development or commercialization of the apoB program. In the event that Genzyme elects option (ii) above, such actions would not affect any of the economic rights that the successor to Isis would otherwise hold. For the purposes of this Term Sheet, a Change of Control shall mean (a) the acquisition by any person or group of Control of Isis or (b) any direct or indirect sale, lease, exchange, or other transfer by Isis of substantially all of the assets to which this Term Sheet relate (but not including any financial factoring agreement). Control means the ownership of, directly or indirectly, at least 50% of the shares of such equity entitled to vote on the election of directors.

Attachment A
Definition of Program Costs

"Program Costs" means all costs and expenses incurred by Genzyme or Isis in connection with the development, manufacture, promotion and sale of the Product, including internal and external costs, as described in more detail below. All Program Costs will be based on each Party's accounting records as maintained in accordance with U.S. GAAP consistently applied.

The following items will be excluded from Program Costs:

- the first $75 million of external development expenses that Isis will fund as described under "Development and Commercialization Roles and Responsibilities" in the term sheet
- the purchase price for the Shares, license fee or milestones payable to Isis
- the costs of the mutually agreed to research program described under "Research Support" in the term sheet
- the costs to prosecute and maintain Patents
-   costs associated with stock-based compensation expenses or other pro forma adjustments to either Party's GAAP financials
- Isis' internal costs for any year in which Program Costs exceed Net Program Revenues (to the extent of such excess).

Program Costs are grouped into the categories described below. Each of the categories below includes bot h internal and external costs unless specifically stated otherwise. The calculation for internal costs is described in the section titled "Internal Costs". In addition, each category includes the allocation of indirect costs as described in the section titled "Indirect Costs". The following is a brief explanation of each of these categories.

Indirect Costs

Indirect costs are the costs for facilities, utilities, insurance, facility and equipment depreciation/amortization and other fixed costs directly relat ed to the conduct of the activities described in each of the categories below and allocated based upon the proportion of such costs directly attributable to the performance of the activities described under each category below or by such other cost allocation method as may be mutually agreed to by the Parties.

Internal Costs

Internal costs consist of the base salary plus a factor for reasonable and customary employee benefits and payroll taxes for those employees directly responsible for performing the activities described in each of the categories below. In the case of commissioned sales personnel performing activities under Sales and Marketing expenses below, internal costs will include the commissions paid to such personnel.

Cost of Goods Sold (COGS)

COGS consists of those standard manufacturing costs routinely included in COGS as defined by U.S. GAAP, including the cost of raw materials, manufacturing labor and related manufacturing overhead. COGS also includes manufacturing variances typically included in COGS under U.S. GAAP. Additionally, COGS includes costs, such as royalties, milestones and license fees, paid to third parties including those currently owed to [***] and [***]. In calculating COGS, the Parties shall use the same assumptions, allocations and calculations as each uses in preparing its publicly reported financial statements and shall allocate to cost categories in a manner consistent across all pharmaceutical product lines without discrimination against Isis products versus Genzyme and its Affiliates' internal products or other products licensed from Third Parties. Notwithstanding the foregoing, COGS does not include costs that are applicable to manufacturing buildings, space or equipment that will not be used to support the manufacturing process during the Firm Order period or that are projected to be underutilized in the manufacturing process due to lower planned capacity versus normal plant capacity. Additionally, COGS does not include the cost of worn-out facilities or equipment, previously used in manufacturing but no longer in operation, or the cost of scrapping and abandoning such assets. Expense items related to the manufacturing operations that are of a non-recurring nature such as equipment or facility design changes, alterations,

disassembly, moving, reinstallation and reassembly of machinery and equipment will be included in the cost of capital projects and amortized into COGS according to the Parties amortization practices under U.S. GAAP. Further, the Parties anticipate that Genzyme will build manufacturing capability to manufacture API for commercial supply. If Genzyme does

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not do so, and a third party is required to manufacture API the portions of API cost reasonably calculated to represent profit and amortization of facility and equipment will not be included in Program Costs. To the extent that Isis manufactures API for the initial launch of the Product, COGS will be Isis' fully burdened cost, as calculated on an annual basis and described in the term sheet under "Manufacture of Product".

Sales & Marketing Expenses (S&M)

S&M expenses include costs necessary to market, distribute and sell the Product. This category includes costs such as those for advertising, marketing collateral, samples, promotional materials, distributor fees, contract sales organization payments, field marketing programs, market research, outside educational programs, printing, publishing, speaker programs, medical education programs, trade shows and exhibits, sales training meetings and seminars, reasonable travel and entertainment costs, translations, reimbursement services, reasonable patient support services, website development and maintenance, call center costs, toll-free phone costs and product liability insurance costs.

Development Expenses

Development expenses include the costs of all clinical trials and preclinical studies, including post-marketing trials, as detailed in the budget attached to the Development Plan. The types of expenses included in this category are investigator grants, laboratory services, clinical PK assays, CRO services and pass-throughs, costs for packaging, distribution and reconciliation (including labels and translations, inventory control, IVRS, off-site storage and destruction), data management (including EDC), clinical study reports, drug costs (API & DP), investigator meetings, monitoring, SAB costs, DSMB costs, key opinion leader costs, program specific travel, metabolomics assays, courier services and clinical trial liability insurance costs. Development expenses inclu de Quality Assurance costs for auditing clinical trial activities and preclinical studies support (report reviews and CMC review). To the extent that Isis manufactures API for clinical trials or preclinical studies of the Product, the cost of the API will be Isis' fully burdened cost, as calculated on an annual basis and described in the term sheet under "Manufacture of Product".

Regulatory Expenses

Regulatory expenses include those costs associated with obtaining and maintaining regulatory approvals for the Pr oduct. They include costs such as regulatory consulting, filing fees, eCTD costs and other publishing costs. They also include costs associated with safety reporting and pharmacovigilance.

Non-COGS Manufacturing Expenses (Non-COGS Mfg)

Non-COGS manufacturing expenses include costs such as those for ongoing stability testing, drug substance and drug product registration stability testing, transfer of API and drug product release and in-process methods, validation of analytical methods, regulatory support and photostability tes ting. Additionally, this category includes costs incurred for NDA supporting studies such as pH rate profile, pH solubility profile, freeze and thaw stability, terminal sterilization and shipping studies. Non-COGS manufacturing expenses also include process justification work for API and DP to support regulatory filings, costs associated with writing development history documents, costs incurred to add additional supply chain vendors as demands increase and tech transfer for API and drug product to Genzyme. Non-COGS manufacturing costs also include any other costs necessary to produce and maintain a CMC document to support product manufacturing.

Other Expenses

Other expenses include costs such as those associated with licensing or actions to pursue an infringer that are mutually agreed to by the Parties. Program Costs will not include the costs to prosecute and maintain Patents. To the extent that there are royalties, milestones and/or license fees owed to third parties that cannot be included in COGS under U.S. GAAP, they will be included in Program Costs within this category. This category would also include foreign currency gains/losses. This category also includes costs specifically identifiable to the Product, which do not fit in any other category.

Attachment B

[***]

Exhibit C

Research Term Sheet

CONFIDENTIAL

EXHIBIT C

Research Term Sheet

Isis Pharmaceuticals and Genzyme

January 7, 2008

This term sheet outlines principal business terms for an agreement (the "Research Option Agreement") between Isis and Genzyme whereby Genzyme will be granted the option to license certain Isis drugs. Genzyme will have the exclusive right to license drugs that become Development Candidates in Isis' neuro-degenerative and rare disease programs for the next two years.

Capitalized terms used but not defined in this Research Term Sheet are used with the meanings given to them in the License and Research Agreement.

Overview of Isis-Genzyme Research Relationship:

- Isis has or will establish research programs in the Exclusive Therapeutic Areas which are described in the attached Exclusive Research Program description. During the Research Period, Isis will continue these programs for the purpose of discovery of Compounds suitable for development and commercialization for human therapeutic uses.

- Genzyme will have the right to recommend specific targets for the Exclusive Research Programs and to contribute to the research strategy as appropriate. In addition, Genzyme will provide Isis access to certain animal models for use in Exclusive Therapeutic Areas. The Exclusive Research Program will be reviewed every [***] months on a formal basis with Genzyme and it is anticipated that it will be discussed on an informal basis more frequently.

- For a [***] period from the Effective Date of the License and Research Agreement, Genzyme will have the option to fund development of any Development Candidate arising out of the Exclusive Research Programs and to license any such Funded Development Candidates after clinical proof-of-concept study(ies) have been completed. Terms for any such licenses will be negotiated in good faith using the basic principles articulated in this term sheet. After licensing a Funded Development Candidate, Genzyme will be solely responsible for the further development and commercialization worldwide.

- Isis currently has two advanced programs in neuro-degenerative disease for [***] and [***]. Genzyme's decision to fund each of these programs will be deferred to the time the current funding is exhausted (end of initial Phase 1 clinical study for [***] and completion of IND supporting toxicology studies for [***] [***]) and any licenses for such programs will reflect the advanced status of these programs and the independent funding thereof.

- At the end of the Research Period , Genzyme will have the right, but not the obligation, to extend the Research Period for up to three years by agreeing to fund a continued Exclusive Research Program agreed upon by both parties at Isis' fully burdened cost.

Joint Research Committee

- A joint research committee will be formed to meet on a regular basis to review the work conducted in the Exclusive Research Program.

Exclusive Research Programs:

- Isis will conduct the Exclusive Research Program at Isis' expenseduring the Research Period which will include activities up to the designation of a Development Candidate (a Compound ready for the initiation of IND-supporting studies for all programs except [***] and [***] [***] which now include activities that are currently covered by outside funding).

- At the time Development Candidate status is attained, Genzyme will have [***] to determine if it would like to advance this Development Candidate forward through clinical proof-of-concept trials. If Genzyme determines that it wants to advance the Development Candidate, it will fund all development work through clinical proof-of-concept (criteria to be mutually defined by Isis and Genzyme prior to initiation of development work), unless otherwise agreed upon by the Parties. These development activities may be conducted by Genzyme or Genzyme may contract with Isis to conduct the work at Isis' fully-burdened cost. After achievement of the pre-determined clinical proof-of-concept, Genzyme will have [***] to determine if it would like to exercise its option to license the Funded Development Candidate.

- The terms for any license will be negotiated in good faith at whatever time Genzyme requests which can be as early as the funding decision at Development Candidate status. Any Compound that either reaches Development Candidate status and Genzyme decides not to fund or that reaches clinical proof-of-concept and Genzyme does not license, will belong to Isis with no further obligations to Genzyme. The scope of any such license would be similar to the scope of the Product License for mipomersen, including the components of the licensed intellectual property.

- The research relationship is focused on delineated Exclusive Therapeutic Areas. Nevertheless, Genzyme's license to any drugs arising there from will not be limited to the Exclusive Therapeutic Areas. Similarly Isis and its partners conduct research programs which, during any period of Genzyme's exclusivity under the terms of this agreement will not be directed to the Genzyme Exclusive Therapeutic Areas but drugs arising out of those programs may similarly be developed and commercialized for any indication.

- As part of the Exclusive Research Program, the [***] Isis development program is being included in the neuro-degenerative disease area. It should be noted that the advanced stage of this program will require Genzyme to make a decision as to whether to fund

early clinical development so as to fit in the option process described above and that any licensing terms will take into account the advanced stage of the drug and Isis' funding thereof.

- Similarly, Isis will be including its [***] program into the Exclusive Research Program. The advanced stage of this program will require Genzyme to make a development funding decision prior to initiation of Phase 1 studies.

Exclusive License:

- Unless otherwise agreed upon by the Parties, upon granting of a license to any Funded Development Candidate that Genzyme has an option to license, Genzyme will be solely responsible, including responsibility for all funding, resourcing and decision-making, all further clinical development, manufacturing (with Isis providing the initial clinical supply), regulatory and commercialization activities for Licensed Compounds and Licensed Products. Upon request by Genzyme, Isis would provide consulting and technical support relating to the Licensed Compounds and Licensed Products.

(i) Manufacturing

- Genzyme will have the option to manufacture Licensed Compounds and Licensed Products; At Genzyme's request, Isis will manufacture and sell to Genzyme pre-clinical and clinical API for each Funded Development Candidate through clinical proof-of-concept trial at the standard rate and upon standard terms Isis charges its other partners, which represents a good faith estimate of fully-burdened cost determined annually. Genzyme will be responsible for DP manufacturing.

- In the case where Isis is unable or for any reason otherwise fails to supply API to Genzyme, upon written request by Genzyme, Isis shall transfer to Genzyme all documentation and information, and permit Genzyme to reference and use any regulatory filings, and otherwise fully cooperate with Genzyme to enable Genzyme to make or have made API for use by Genzyme.

Intellectual Property

- Following license of a Compound to Genzyme, Isis will assign to Genzyme all Isis Product Specific Patents relating to Licensed Products and their gene targets. Isis will be responsible for filing and prosecuting all Core Technology Patents and any other patents owned or controlled by Isis.

- Isis will agree to consult with Genzyme on prosecution and filing decisions after Genzyme opts to fund work following Development Candidate status on patents relating to such Development Candidate.

- The Parties will cooperate to obtain new licenses under any third party patents that are necessary for the development, manufacture and commercialization of the Licensed Product.

- Inventions conceived solely by Isis shall be documented, processed and owned by Isis.

- Inventions conceived solely by Genzyme shall be documented, processed and owned by Genzyme.

- Inventions conceived jointly, as deemed by the U.S. laws of inventorship, by Genzyme and Isis shall be documented, processed and owned equally by both organization.

    - In the event that a third party is interested in licensing an invention that was developed jointly under this agreement and is applicable only in the Exclusive Therapeutic Area, both Genzyme and Isis must agree to the terms of the license.

Certain Definitions:

"Compound" means any oligonucleotide acting by [***] that arises from the Exclusive Research Program during the Research Period.

"Development Candidate" means any Compound that has been deemed by Isis ready to start IND-enabling toxicology studies in accordance with its standard process.

"Effective Date" has the meaning given to it in the License and Research Agreement.

"Exclusive Therapeutic Area" means the therapeutic areas of neuro-degenerative and certain rare diseases to be mutually agreed upon by the Parties.

"Exclusive Research Program" means the research program being performed by Isis pursuant to the Research Plan to identify Development Candidates in the Genzyme Exclusive Therapeutic Areas.

"Funded Development Candidate" means any Development Candidate that has been funded by Genzyme for preclinical toxicology and early clinical studies.

"Research Period" means the two year period in which Isis will conduct the Exclusive Research Program.

Genzyme-Isis Drug Discovery Exclusive Research Program Description

January 7, 2008
[***]

Exhibit D

Disclosure Schedule

[***]

CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R §§ 200.80(b)4, AND 240.24b-2

EXECUTION VERSION *(02/08/08)*

AMENDED AND RESTATED COLLABORATION AND LICENSE AGREEMENT

This Amended and Restated Collaboration and License Agreement (the "**Agreement**") between **ISIS PHARMACEUTICALS, INC.** of 1896 Rutherford Road, Carlsbad, CA 92008, USA ("**ISIS**") and **ANTISENSE THERAPEUTICS LTD.,** ACN 095 060 745 of Level 1, 10 Wallace Avenue, Toorak, Victoria 3142, AUSTRALIA ("**ATL**") is entered into and made effective as of February 8, 2008 (the "**Amendment Date**").

INTRODUCTION AND OVERVIEW

ISIS and ATL are parties to that certain Collaboration and License Agreement effective as of December 21, 2001 (the "**Effective Date**"), as amended (the "**Original Agreement**"), pursuant to which, among other things, the parties agreed to collaborate to enable ATL to develop and commercialize antisense drugs, including, without limitation, the Antisense Inhibitor known as ATL 1102 (formerly known as ISIS 107248), VLA4 Compounds and Other VLA4 Compounds.

ATL proposes to enter into a sublicense agreement with Teva Pharmaceutical Industries Ltd. ("**Teva**") in the form provided to ISIS on the Amendment Date (the "**Teva Sublicense**"), pursuant to which ATL would grant to Teva an exclusive, worldwide sublicense to develop and commercialize ATL 1102, VLA4 Compounds and Other VLA4 Compounds, and VLA4 Products, subject to the terms and conditions set forth therein.

As a condition to Teva's willingness to enter into the Teva Sublicense, Teva has requested that ATL and ISIS implement certain amendments to the Original Agreement.

In order to facilitate ATL's entry into the Teva Sublicense, the parties wish to amend and restate the Original Agreement as set forth in this Agreement, effective as of the Amendment Date.

Therefore, in consideration of the foregoing premises and the mutual covenants herein contained, the parties hereby agree as follows.

AGREEMENT

ARTICLE 1

DEFINITIONS

Capitalized terms used in this Agreement have the meanings set forth in Exhibit 1.

ARTICLE 2

DRUG DEVELOPMENT PROGRAM

2.1 General.

Under the Drug Development Program, ATL will develop and commercialize antisense drugs arising out of the Collaborative Research Program conducted hereunder, as well as ATL1102 (a Collaboration Compound discovered by ISIS), VLA4 Compounds and Other VLA4 Compounds and VLA4 Products. In general, ATL will be responsible for all development and commercialization activities for Collaboration Compounds. ISIS has performed, and, pursuant to the Teva/ISIS Agreements, may continue to perform, certain activities in support of the development of ATL1102, VLA4 Compounds and Other VLA4 Compounds, but it is the intent of the parties that ATL will assume responsibility for all preclinical and IND-enabling activities with respect to other Collaboration Compounds, as more specifically provided in this Agreement. ATL will be responsible for all costs of development and commercialization of Collaboration Compounds including, without limitation, the reimbursement of ISIS' expenses as provided herein.

2.2 Development of VLA4 Compounds and Other VLA4 Compounds.

(a) General. ATL will use commercially reasonable efforts to develop at least one VLA4 Compound to maximize its commercial value. ATL will conduct the development of VLA4 Compounds and VLA4 Products in a good scientific manner and in compliance in all material respects with all requirements of applicable laws, rules and regulations to achieve the objective specified in the first sentence of this subsection (a) efficiently and expeditiously. ATL will proceed diligently with the development of VLA4 Compounds and VLA4 Products using commercially reasonable efforts to provide sufficient time, effort, equipment, facilities and skilled personnel.

(b) VLA4 Compound Development Diligence.

(i) During Term of Teva Sublicense. The parties agree that, during the term of the Teva Sublicense: (A) no Development Milestones will be applicable to ATL 1102, VLA4 Compounds, Other VLA4 Compounds or VLA4 Products; (B) the only diligence obligations applicable to the development of ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products will be those set forth in Section 2.2(a) above; and (C) notwithstanding the definition of Active Program set forth in Exhibit 1 hereto, compliance with the diligence obligations set forth in Section 2.2(a) will satisfy the "Active Program" and "Active Development" criteria with respect to ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products.

(ii) After Term of Teva Sublicense. In the event of termination or expiration of the Teva Sublicense prior to Marketing Approval of a VLA4 Product in each of the Major Markets (and prior to the termination or expiration of this Agreement), then ATL and ISIS will, as promptly as practicable, mutually agree in writing upon

Development Milestones for ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products that ATL will commit to reach, in which event the parties agree as follows with respect to such Development Milestones. If a Development Milestone is not met, [***] extension on such Development Milestone, provided that ATL (x) gives the JDC members at least [***] prior written notice that it is unlikely to achieve the relevant milestone on the date specified above, and (y) demonstrates to the JDC that [***] agreed upon by the parties. If the JDC cannot agree on this issue, the matter will be referred to the designated officers of ATL and ISIS for resolution, consistent with the provisions of Section 16.6(a).

2.3 Development of Collaboration Compounds Other Than VLA4 Compounds.

(a) General. The provisions of this Section 2.3 will apply solely to Collaboration Compounds other than ATL 1102, VLA4 Compounds or Other VLA4 Compounds.

(i) As provided herein, during the term of this Agreement, ATL will advance additional Collaboration Compounds through the various stages of an Active Program hereunder, i.e., from the research phase through preclinical and IND-enabling studies to human clinical studies and commercialization. To maintain any Collaboration Compound in Active Development status, ATL must meet the Development Milestones for each such Collaboration Compound.

(ii) The terms under which ISIS and ATL will collaborate to develop such additional Collaboration Compounds will be in accordance with the terms set forth herein. Within 60 days of ATL's providing written notice to ISIS that ATL has initiated IND enabling studies on a Collaboration Compound, ATL will prepare a mutually-agreed-upon Development Plan for that Collaboration Compound, with ISIS' assistance, consistent with the terms of this Agreement.

(b) [***] Studies. While it is the intent of the parties that ATL will assume responsibility for all [***] activities with respect to Collaboration Compounds other than ATL 1102, VLA4 Compounds or Other VLA4 Compounds, ISIS will be available to assist with [***] other than ATL 1102, VLA4 Compounds and Other VLA4 Compounds, if requested to do so by ATL. Should ATL request ISIS' assistance in this regard, the parties will agree on terms pertaining to ISIS' participation, which terms will be included in the Development Plan referenced in (a). With the possible exception of an [***] Collaboration Compound, ISIS will not be requested to participate in the [***].

2.4 Annual Reports.

ATL will provide ISIS with an annual written report describing all activities performed by the parties and the results achieved during the relevant year with respect to each Collaboration Compound in Active Development hereunder including, without limitation, ATL 1102, VLA4 Compounds and Other VLA4 Compounds. Each such report will include details regarding the stage of development a Collaboration Compound has reached within an Active Program including, without limitation, what Development Milestones (if applicable) have been achieved.

To the extent that it is feasible to do so, ATL will also include the projected goals and Development Milestones it anticipates achieving during the coming year with respect to such Collaboration Compound in each such report. Notwithstanding the foregoing, ISIS acknowledges that ATL will not necessarily have access to all information regarding activities conducted by Teva and that this Section 2.4 only obligates ATL to report to ISIS with respect to information known to ATL.

2.5 Commercialization.

(a) General. ATL will use commercially reasonable efforts to bring Products into commercial use as quickly as is reasonably possible, in a manner designed to maximize the commercial potential of such Products worldwide. ATL will use commercially reasonable efforts to Manufacture, market, promote, distribute, and sell the Product on a worldwide basis. ATL will provide resources and expend funds in connection with such activities in a manner and to an extent comparable to the efforts of similar companies that manufacture, market, and sell pharmaceutical products of similar commercial potential at a similar stage of the product life cycle.

(b) Product Plan.

(i) ATL. Except as set forth in subsection (ii) below, prior to the launch of any Product, ATL will prepare a global integrated Product plan outlining the key aspects of market launch and commercialization (the "**Integrated Product Plan**" or "**IPP**"). Each IPP will be updated annually in accordance with ATL's internal planning and budgeting process. ATL will provide ISIS a copy of the final draft of each IPP (original and updates) for each Major Market. Each IPP will also include appropriate milestones and the dates upon which such milestones must be met by ATL.

(ii) Teva and Other Sublicensees. If a Sublicensee of ATL (including Teva) bears primary responsibility for commercialization of any Product in one or more Major Markets, then ATL need not prepare an IPP covering such Product in such Major Market(s) and any other territory in which such Sublicensee has primary commercialization responsibility (collectively, the "**Sublicensee Market**"); *provided, however,* that:

(A) the sublicense agreement between ATL and such Sublicensee will require that, prior to the launch of any Product, such Sublicensee will prepare a written plan outlining the key aspects of market launch and commercialization of such Product in the Sublicensee Market (a "**Sublicensee Product Plan**" or "**SPP**"), which will be updated at least annually;

(B) ATL will provide ISIS with true and complete copies of each SPP and update thereto that ATL receives, whether in draft or final form, promptly following receipt thereof from the Sublicensee; and

(C) the sublicense agreement between ATL and such Sublicensee will expressly provide that (1) ATL is permitted to transmit copies of all SPPs and updates thereto to ISIS; (2) [***] (3) such Sublicensee will [***]

(c) Commercialization by Sublicensees. If a Sublicensee of ATL bears primary responsibility for commercialization of any Product in the applicable Sublicensee Market, the sublicense agreement will require that such Sublicensee will use commercially reasonable efforts to Manufacture, market, promote, distribute, and sell the Product in such Sublicensee Market and will require that the Sublicensee provide resources and expend funds in connection with such activities in a manner and to an extent comparable to the efforts of similar companies that manufacture, market, and sell pharmaceutical products of similar commercial potential at a similar stage of the product life cycle. Consistent with Section 4.3 below, if ATL elects to meet any of its responsibilities and obligations under this Section via sublicense agreements, ATL will ensure that such agreements are subject to and will be consistent with the terms and conditions of this Agreement including, without limitation, the provisions of this Section.

(d) Failure to Meet Diligence Obligations. If ATL or a Sublicensee of ATL anticipates any difficulty in meeting its commercialization obligations under this Section including, without limitation, the milestones set forth in the IPP, ATL or its Sublicensee will provide ISIS with prompt notice thereof, in order that the parties may endeavor to work out an appropriate and acceptable resolution prior to pursuing other remedies hereunder.

(e) Acknowledgment Regarding Teva Sublicense. ISIS acknowledges and agrees that the Teva Sublicense, in the form provided to ISIS on the Amendment Date, satisfies the requirements of this Section 2.5 applicable to sublicense agreements between ATL and Sublicensees.

2.6 Effect of Change of Control and Competing Products

(a) Change of Control of ATL: ISIS acknowledges and agrees that, notwithstanding anything else in this Agreement, if a Change of Control of ATL in which the Third Party acquiring control of ATL or its assets relating to VLA4 Products is a [***], then:

(i) ATL will procure that Teva's reports regarding any development plan, commercialization plan or SPP relating to VLA4 Products will be provided by Teva directly to ISIS; and

(ii) for so long as Teva provides such reports, ATL will not be required to separately provide to ISIS annual reports and other information relating to the development and commercialization of VLA4 Products.

(b) Change of Control of ISIS. Notwithstanding anything contained herein to the contrary, in the event of a Change of Control of ISIS in which [***] then:

(i) ISIS (or the successor entity) will not be allowed to [***] and

(ii) ATL will not be required to provide to ISIS (or the successor entity) with any [***], other than (A) reports and information required to be made available under Sections 5.6 and 5.8 of this Agreement and (B) summary annual reports regarding Teva's development and commercialization activities with respect to VLA4 Products in sufficient detail to allow ISIS to ascertain ATL's compliance with its diligence obligations under this Agreement.

(c) Competing products: ISIS acknowledges and agrees that if ATL Exploits a product that is [***], then:

(i) ATL will procure that Teva's reports regarding any development plan, commercialization plan or SPP relating to VLA4 Products will be provided by Teva directly to ISIS; and

(ii) for so long as Teva provides such reports, ATL will not be required to separately provide to ISIS annual reports and other information relating to the development and commercialization of VLA4 Products.

ARTICLE 3

COLLABORATIVE RESEARCH PROGRAM

3.1 General; Collaboration Term.

(a) ATL and ISIS will work together under the Collaborative Research Program described herein and as further detailed in the Collaborative Research Plan, as described in Section 3.2, to discover and develop antisense therapeutics. The parties will collaborate to assess Research Targets that may be important in the prevention or treatment of a disease or condition, consistent with Sections 3.2 - 3.5. If contracted by ATL, ISIS will discover and design antisense oligonucleotides to modulate the Research Targets as provided in Section 3.6 and will provide them to ATL. Also, if contracted by ATL, ISIS will evaluate the antisense oligonucleotides in various functional assays. ATL will perform *in vitro* and *in vivo* studies utilizing the antisense oligonucleotides provided by ISIS. It is the intent of the parties that Collaboration Compounds will be identified during the Collaboration Term and that pursuant to Active Programs hereunder, such Collaboration Compounds will progress through research and preclinical development, meeting the relevant Development Milestones (see Exhibit 1, Section 1.2), and will each become the focus of a Development Plan hereunder, except as expressly set forth in Section 2.2(b) hereof.

(b) The Collaboration Term will begin on the Effective Date and will continue until December 21, 2008, unless earlier terminated due to termination of the Agreement under Sections 12.2 or 12.3, or unless terminated or extended upon mutual agreement of the parties.

3.2 Joint Research Committee.

(a) The parties have established a Joint Research Committee of 4 people, consisting of 2 representatives nominated by each party, to facilitate the research collaboration called for herein. Each party will designate a representative as a project leader to serve as the principal contact person for that party. The parties may agree to add additional members to the JRC, as long as equal representation is maintained. As ISIS' participation will largely be to [***] will designate one of its representatives as chairman of the JRC. In the event of a tied vote, [***] will have the tie-breaking vote.

(b) During the Collaboration Term, the JRC will be the primary vehicle for interaction between the parties with respect to the collaborative research conducted hereunder. The JRC will be responsible for preparing an annual budget and plan for the collaborative research activities to be conducted during each year of the Collaborative Research Program (the "Collaborative Research Plan") and for managing that program. The JRC will be responsible for updating the Collaborative Research Plan as needed and will also be responsible for prioritizing work contracted to ISIS under Section 3.6.

(c) The JRC will meet as needed during the Collaboration Term. Meetings will be via teleconference or videoconference, or as the parties may otherwise agree. The JRC will review the progress of the activities carried out under the Collaborative Research Program and will consider and decide on proposed modifications to the strategy and goals of that program. The frequency, dates and times of all meetings will be mutually agreed upon by the parties. At its first meeting the JRC will determine such procedures as it will reasonably require to conduct its business.

3.3 Research Targets: General.

As noted above, ATL and ISIS will collaborate to assess Research Targets that may be important in the prevention or treatment of a disease or condition.

3.4 Research Targets: Designation.

(a) The collaborative research hereunder will be focused on specific gene targets thought to be attractive for the development of antisense drugs. ATL will choose targets in accordance with the provisions of this Section 3.4 as the basis for its antisense drug discovery efforts. ATL commits to use commercially reasonable efforts to conduct research and drug discovery activities with respect to each Research Target to maximize its commercial value.

(b) Exhibit 3.4 hereto contains a list of the targets that are the object of Licenses to Research as of the Amendment Date (the "**Research Targets**"), as well as [***] Research Targets listed on Exhibit 3.4 that are [***] Targets are listed in Section B, and all other Research Targets are listed in Section A of Exhibit 3.4. During the Collaboration Term, targets may be added to and removed from Exhibit 3.4 in accordance with the terms of this Section and Section 3.5.

3.5 Research Targets: Selection, Removal, Replacement and Approval Process.

(a) Exhibit 3.4 lists the Research Targets agreed upon by the parties as of the Amendment Date. ATL warrants and represents that if it has not provided ISIS with the nucleic acid sequences for the corresponding human genes for any of the Research Targets listed in Exhibit 3.4 by the Amendment Date, it will do so promptly thereafter. Consistent with the terms of this Agreement, ISIS will have no obligation to conduct any activities with respect to such Research Targets until the required materials, information and/or payments (if applicable) have been submitted to ISIS by ATL. The addition of new Research Targets to the list in Exhibit 3.4 is at ISIS' sole discretion.

(b) If ATL wishes to designate a new Research Target, it will provide ISIS with written notice of the target it wishes to add to the list set forth in Exhibit 3.4. Such written notice will include the gene name, the NCBI accession number or nucleic acid sequence, and one or more mammalian cell lines that express the Research Target. ISIS will not, and is not required to, accept a proposed Research Target without such information. In addition, ATL will inform ISIS of whether or not to the best of ATL's knowledge the proposed target is in the public domain or is proprietary to a Third Party.

(i) ATL will not propose a target for consideration as a possible Research Target if [***].

(ii) If ATL proposes a target that is [***], but ATL is able to provide ISIS with [***] the proposed target, ATL will also provide ISIS with a copy of any [***] ATL also warrants that any [***] required to be made to a Third Party in order to [***] activities in support of the Collaborative Research Program will be the sole responsibility of ATL. For the purpose of this Section, Third Party restrictions do not include [***].

(iii) If a target proposed by ATL is subject to an ISIS drug discovery and development program or a contractual obligation of ISIS to a Third Party with respect to that target, then the proposed target will not be approved as a Research Target hereunder.

(c) Within [***] days after receipt of the ATL notice under subsection (b), ISIS will notify ATL, in writing, of its decision either to approve or to reject a proposed target.

(i) If a proposed target is not approved as a Research Target, the notice provided by ISIS will advise ATL of the reason(s) the target was not approved, and ATL will be invited to submit a different proposed target for consideration.

(ii) If a proposed target is approved as a Research Target, ISIS' notice to ATL will indicate this and will also indicate whether or not the new Research Target is a [***] Target. ISIS will add the Research Target to the list in Exhibit 3.4 (as well as the nucleic acid sequence of the gene) and will provide ATL with an amended copy of Exhibit 3.4. If ISIS has [***], ISIS will add that information to Exhibit 3.4 and will provide ATL with a copy of the amended exhibit.

(iii) Upon receipt of written notice from ISIS that a proposed target has been approved as a Research Target and added to Exhibit 3.4, ATL will begin Active Development of such Research Target, consistent with the terms of this Agreement.

(d) After the Effective Date, Research Targets may be removed from the list in Exhibit 3.4 as follows.

(i) If ATL wishes to remove a Research Target from the approved list in Exhibit 3.4, it will provide ISIS with prompt written notice of its election to do so. Upon ISIS' receipt of such notice, it will remove the Research Target from the list.

(ii) Upon receipt of notice at any time during the term of this Agreement that a Research Target is no longer in Active Development, ISIS will remove the target from the list set forth in Exhibit 3.4 and will provide ATL with prompt written notice of same.

(iii) The License to Research or License to Exploit applicable to any Research Target removed pursuant to (i) or (ii) herein (each an "Abandoned Research Target") will immediately terminate, consistent with the provisions of Sections 4.1 or 4.2, as applicable. Notwithstanding the foregoing, an Abandoned Research Target may still bear royalty or other payment obligations, as described in Sections 5.1 – 5.3 herein.

(iv) Once a target has been removed from the list of Research Targets, Exhibit 3.4 will be amended to delete such target and a copy of amended Exhibit 3.4 will be sent to ATL by ISIS.

(v) Upon termination of a License to Research or a License to Exploit for any reason, a Research Target will be automatically removed from Exhibit 3.4 and will thereafter be considered an Abandoned Research Target.

(e) At no time during the term of this Agreement or the Collaboration Term will there be any more than [***] designated Research Targets. ATL may not substitute more than [***] Research Targets in any year during the Collaboration Term.

3.6 Discovery and Evaluation of Antisense Inhibitors.

(a) Research Services. During the Collaboration Term, ATL may request from time to time that ISIS perform Research Services with respect to one or more Research Targets. If ISIS agrees to provide any requested Research Services to ATL, such Research Services will be described in a written work plan to be negotiated in good faith by the parties, which would include the compensation to be made by ATL for such Research Services. ATL will be responsible for conducting further in *in vitro* and *in vivo* studies of Antisense Inhibitors provided by ISIS as a result of such Research Services. The number, quantity and price of Antisense Inhibitors to be provided by ISIS to ATL for use in such studies will be set forth in the applicable work plan. If ATL requests additional quantities of any such Antisense Inhibitor, the terms of supply will be mutually agreed upon by the parties

in writing. The ownership and use of all materials, including Antisense Inhibitors, and of all data and information generated as a result of services provided to ATL by ISIS pursuant to this Agreement is governed by the provisions of Article 6. There will be no minimum or maximum amount of Research Services that ATL is obligated or entitled to request or ISIS is obligated or entitled to provide.

(b) Project Coordinators. ATL and ISIS will each select one employee to serve as the Project Coordinator for that party, with respect to services to be performed under Section 3.6(a). The Project Coordinators will facilitate the selection, prioritization, removal and replacement of Research Targets. The Project Coordinators will each have appropriate technical credentials, knowledge and ongoing familiarity with the foregoing activities. The Project Coordinators will meet on an as-needed basis via teleconference or videoconference, at times mutually agreed upon by the parties. Decisions of the Project Coordinators will be unanimous. If the Project Coordinators cannot agree on an issue, the issue will be submitted to the JRC for resolution.

3.7 Other Collaborative Research Program-Related Activities.

(a) During the Collaboration Term, ISIS will provide ATL with reasonable amounts of preclinical and research advice free of charge (phone consultation or visit at ISIS only) in support of any Active Program hereunder that involves a Collaboration Compound made using ISIS Standard Chemistry for which a License to Research exists.

(b) If ATL requests additional amounts or types of consulting support or training not specified above in this Article 3 and if ISIS agrees to provide such support or training, the parties will negotiate appropriate terms including, without limitation, the scope, timing, duration and cost of such support or training, in good faith.

ARTICLE 4

LICENSE GRANTS AND OTHER RIGHTS

4.0 License Term. As used herein, "License Term" means the term beginning on the Effective Date and ending on the date on which all obligations to pay royalties hereunder have expired.

4.1 Licenses to Research. A License to Research is a license to perform research and development activities relating to a Research Target until the filing of an NDA or non-US equivalent on a Product that modulates such Research Target.

(a) License Grant.

(i) For each Research Target, ISIS will grant to ATL and its Affiliates when ATL takes a License to Research, an exclusive, worldwide license under the ISIS Core Technology Patent Rights, the ISIS Formulation Patent Rights, the Manufacturing Patent Rights, the Research Target

Patent Rights and the Third Party Patent Rights solely to conduct research and clinical development for all human indications for Collaboration Compounds that modulate such Research Target.

For Collaboration Compounds that modulate Dermatology Targets, the license is limited to topical dermatological indications only. These rights will only be sublicensable as explicitly provided in Section 4.3. The license grant described hereunder will commence automatically on grant of the License to Research and will terminate upon termination of the corresponding License to Research.

(ii) For each Research Target, ISIS will grant to ATL and its Affiliates when ATL takes a License to Research, a nonexclusive, worldwide license under the Research Target Patent Rights, the ISIS C5-Propyne Patent Rights, and the ISIS Formulation Patent Rights solely to conduct research and clinical development for all therapeutic and cosmetic applications for Research Target Compounds that modulate such Research Target. For Research Target Compounds that modulate Dermatology Targets, the license is limited to topical dermatological indications only. These rights will only be sublicensable as explicitly provided in Section 4.3. The license granted hereunder will commence automatically on grant of the License to Research and will not terminate upon termination of the corresponding License to Research.

(b) As of the Amendment Date, ISIS grants to ATL a License to Research with respect to each Research Target listed in Exhibit 3.4. ATL will receive additional Licenses to Research with respect to Research Targets when added to Exhibit 3.4. Licenses to Research may only be obtained during the Collaboration Term. No License to Research will be granted to ATL on any Research Target after the Collaboration Term ends.

(c) [***].

(d) ATL may terminate a License to Research with respect to a Research Target for any reason, at any time during the term of this Agreement, by providing ISIS with written notice that the Research Target is being removed from Exhibit 3.4.

(e) With the exception of the License to Research applicable to ATL 1102, VLA4 Compounds and Other VLA4 Compounds, which is governed by the provisions of subsections (f) and (g) below, if a Research Target is no longer part of an Active Program, ISIS may terminate the License to Research applicable to that Research Target at any time during the term of this Agreement upon written notice to ATL.

(f) Once ATL has elected and obtained [***] Licenses to Exploit pursuant to Section 4.2, all remaining Licenses to Research will immediately terminate, and all rights to the remaining Research Targets licensed to ATL will revert to ISIS; provided, however, that the licenses granted pursuant to Section 4.1(a)(ii) will remain in effect.

(g) ISIS will provide ATL with a semiannual report summarizing the status of Research Target Patent Rights subject to a License to Research hereunder and will include updates to any Exhibits that are affected.

4.2 Licenses to Exploit. A License to Exploit is a license to perform research, development and commercialization activities on, and otherwise Exploit, Products that modulate a Research Target.

(a) ISIS grants ATL the option to convert any active License to Research hereunder into a License to Exploit, as set out below. Notwithstanding the foregoing, ATL may convert not more than [***] Licenses to Research into Licenses to Exploit, and each License to Exploit must be requested by ATL prior to the filing of an NDA (or non-US equivalent) for the relevant Research Target. The option to convert Licenses to Research to Licenses to Exploit expires [***] years after the end of the Collaboration Term.

(b) If ATL elects to convert a License to Research into a License to Exploit, ATL will provide ISIS with written notice effecting the exercise of the option, which will identify the particular Research Target to which the License to Research applies and will include written verification that all applicable milestones and obligations of ATL with respect to that Research Target have been timely met. Upon ISIS' receipt of such written notice, ISIS will have [***] days to object if it believes that ATL has not timely met all applicable milestones and obligations with respect to that Research Target. At the end of such [***]-day period, the License to Exploit will be granted with respect to the relevant Research Target if ISIS has not objected. [***].

(c) <u>License Grants and Assignments.</u>

(i) VLA4 Compounds and Other VLA4 Compounds.

(A) Subject to the terms and conditions of this Agreement, effective as of the Amendment Date, ISIS hereby grants to ATL an exclusive, worldwide license under the ISIS Core Technology Patent Rights, the ISIS Formulation Patent Rights, the Manufacturing Patent Rights, the Research Target Patent Rights (other than the VLA4 Compound Patent Rights, which are covered by Section 4.2(c)(i)(C) below) and the Third Party Patent Rights solely to Exploit ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products for all human indications. These rights will only be sublicensable as explicitly provided in Section 4.3. This license will terminate only in accordance with Section 12.2 hereof.

(B) Subject to the terms and conditions of this Agreement, effective as of the Amendment Date, ISIS hereby grants to ATL a nonexclusive worldwide license under the ISIS [***] and the ISIS Formulation Patent Rights to Exploit ATL1102, Other VLA4 Compounds and VLA4 Products for all human indications. These rights will only be sublicensable as explicitly provided in Section 4.3. This license will terminate only in accordance with Section 12.2 hereof.

(C) Subject to the terms and conditions of this Agreement (including, without limitation, Section 4.8(c) hereof), effective as of the Amendment Date, ISIS hereby assigns to ATL all of ISIS' right, title and interest in and to the VLA4 Compound Patent Rights.

ISIS agrees to execute all assignment and other documents, testify and take all other actions reasonably necessary or appropriate to transfer, effect, confirm, perfect, record, preserve, protect and enforce ATL's right, title and interest in the VLA4

Compound Patent Rights throughout the world, at the reasonable request and expense (to the extent of any out-of-pocket costs incurred by ISIS) of ATL. ATL covenants not to sell, transfer or assign any of the VLA4 Compound Patent Rights to any Affiliate or Third Party, except in connection with a permitted assignment by ATL of this Agreement and ATL's rights and obligations hereunder to an Affiliate or Third Party in accordance with Section 16.2.

(D) Isis hereby covenants that for so long as the licenses granted in Sections 4.2(c)(i)(A) and 4.2(c)(i)(B) above remain in effect, Isis will not [***] with respect to [***] however, if a VLA4 Product has not [***] (or such later date as is mutually agreed by the parties), then [***] will terminate as of such date.

(ii) Other Research Targets and Collaboration Compounds.

(A) For each Research Target (other than CD49d) for which a License to Exploit is granted ISIS will grant to ATL an exclusive, worldwide license under the ISIS Core Technology Patent Rights, the ISIS Formulation Patent Rights, the Manufacturing Patent Rights, the Research Target Patent Rights and the Third Party Patent Rights solely to develop, make, have made, use, sell, have sold, offer for sale and import Collaboration Compound Products that modulate such Research Target for all therapeutic and cosmetic applications. For Collaboration Compound Products that modulate [***], the license is limited to [***] only. These rights will only be sublicensable as explicitly provided in Section 4.3. This license will commence automatically on grant of the corresponding License to Exploit and will terminate upon termination of the corresponding License to Exploit.

(B) For each Research Target (other than CD49d) for which a License to Exploit is granted ISIS will grant to ATL a nonexclusive worldwide license under the [***] and the [***] solely to develop, make, have made, use, sell, have sold, offer for sale and import Research Target Compound Products for all therapeutic and cosmetic applications. For Research Target Compound Products that modulate [***], the license is limited to [***] only. These rights will only be sublicensable as explicitly provided in Section 4.3. This license will commence automatically on grant of the corresponding License to Exploit and will not terminate upon termination of the corresponding License to Exploit.

(d) No substitutions may be made on Licenses to Exploit. Once a License to Exploit has been taken with respect to a Research Target, a different Research Target may not be substituted thereunder.

(e) Subject to the terms and conditions of the Teva Sublicense, ATL may terminate a License to Exploit with respect to a Research Target, for any reason, at any time during the term of this Agreement, by providing ISIS with written notice.

(f) The party bearing primary responsibility for the prosecution, maintenance and defense of any Research Target Patent Rights pursuant to Article 8 herein will provide the other party hereto with a semiannual report summarizing the status of Research Target Patent Rights subject to a License to Exploit hereunder for which such party is responsible and will include updates to any Exhibits listing rights in any Patents licensed hereunder that are affected, if appropriate.

4.3 Sublicenses Under ISIS Patent Rights and Third Party Patent Rights.

(a) Any sublicense granted by ATL and its Affiliates under this Agreement is subject to and will be consistent with the terms and conditions of this Agreement and with the terms of the agreements pursuant to which ISIS obtained its rights in Third Party Patent Rights. The grant of any such sublicense hereunder will not relieve ATL or its Affiliates of its obligations under this Agreement. ATL will promptly provide ISIS with copies of all sublicenses granted by ATL or its Affiliates (including, without limitation, the Teva Sublicense), as well as Sublicensee contact information.

(b) Subject to the terms and conditions of this Agreement and during the License Term, ATL and its Affiliates will have the right to grant sublicenses (each an "**ATL Sublicense**") under the licenses from ISIS set forth in Sections 4.1 and 4.2 to Third Parties as follows.

(i) Teva Sublicense.

(A) ATL may enter into the Teva Sublicense, in the form provided to ISIS on the Amendment Date.

(1) ATL hereby covenants that, except with ISIS' prior written consent, ATL will not amend the Teva Sublicense in any manner that would (a) conflict with this Agreement, (b) expand the scope of the sublicense granted to Teva under ATL's rights hereunder to include any compound or product other than ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products; (c) diminish any rights of ATL thereunder that would result in any direct or indirect diminution of ISIS' rights under this Agreement, or (d) diminish any rights expressly conferred upon ISIS under the Teva Sublicense. ATL will obtain the written covenant of Teva not to amend the Teva Sublicense in any of the foregoing ways.

(2) Each party to this Agreement hereby covenants that, except with Teva's prior written consent, such party will not amend this Agreement in any manner that would (a) diminish any rights of ATL hereunder that would result in any direct or indirect diminution of Teva's rights under the Teva Sublicense, (b) diminish any rights expressly conferred upon Teva under this

Agreement, or (c) directly or indirectly impose any additional financial or other obligations upon Teva beyond those specified in the Teva Sublicense.

(B) ATL and its Affiliates acknowledge and agree that: (1) the sublicense granted to Teva under the ISIS Core Technology Patent Rights, the ISIS Formulation Patent Rights, the Manufacturing Patent Rights, and the Third Party Patent Rights may be practiced solely for Exploiting the ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products for all human indications; and (2) any further sublicense granted by Teva (or any of its sublicensees) to another Third Party under any of the foregoing Patent Rights will be subject to the restriction set forth in the preceding clause (1). ATL will obtain the foregoing written acknowledgment and agreement from each Sublicensee (including Teva).

(C) In the event of a material default by Teva under the Teva Sublicense, ATL will promptly inform ISIS in writing and take commercially reasonable efforts to cause Teva to cure the default. Alternatively, ATL will have the right to cure such default on Teva's behalf. If ATL elects to cure such default on Teva's behalf, ATL will promptly provide to ISIS a written plan outlining the steps ATL will undertake in order to cure such default, including ATL's good faith estimate of the period of time for ATL to do so. If Teva does not timely cure such material default and ATL does not elect to cure such default on Teva's behalf (or elects to cure such default but does not timely comply with the written cure plan described above), ATL will terminate the Teva Sublicense.

(D) In the event of a material default by ATL under this Agreement that relates to CD49d, ATL 1102 or any VLA4 Compounds, Other VLA4 Compounds or VLA4 Product (including, without limitation, any fundamental breach of this Agreement by ATL with respect to which ISIS provides written notice to ATL under Section 12.2), ISIS will promptly inform Teva in writing (in accordance with the notice provisions of the Teva/ISIS Agreements), and the parties agree that Teva will have the right to cure such default on ATL's behalf.

(E) If Teva wishes to have ISIS generate any Other VLA4 Compound, ISIS will be not obligated to generate any such Other VLA4 Compound unless and until Teva and ISIS mutually agree in writing upon a research plan specifically describing the activities to be undertaken by ISIS, including the amounts to be reimbursed by Teva to ISIS for performing such activities. In addition, to the extent that ATL has the right to develop and commercialize any Other VLA4 Compound, ATL may request that ISIS generate such Other VLA4 Compound in accordance with Section 3.6 hereof.

(F) ATL acknowledges and agrees that this Agreement does not grant to ATL any license or right under ISIS Patent Rights to develop, make, have made, use, sell, have sold, offer for sale or import any [***]. ATL further acknowledges and agrees that if Teva wishes to have ISIS generate any [***], ISIS will be not obligated to generate any such [***] Compound unless and until: (i) Teva and ISIS mutually agree in writing upon a research plan specifically describing the activities to be undertaken by ISIS, including the amounts to be reimbursed by Teva to ISIS for performing such activities; (ii) TEVA and ISIS mutually agree in writing upon license terms [***] with respect to products utilizing the [***]; and (iii) only if and to the extent such [***](s) is(are) within the scope of the license(s) granted by ISIS to ATL hereunder, ATL and ISIS mutually agree in writing upon the [***] would be payable by ISIS to ATL with respect to products developed utilizing such [***].

(ii) Other ATL Sublicenses.

(A) In addition to ATL's right to grant the Teva Sublicense, ATL and its Affiliates may grant an ATL Sublicense to a Third Party collaborator under the Research Target Patent Rights solely for the purpose of enabling such Third Party to collaborate with ATL on bona fide research, development and commercialization work on a Research Target Compound and, after such collaborative work, to make, have made, use, offer for sale and sell a Product containing such Research Target Compound.

(B) ATL and its Affiliates may grant an ATL Sublicense to a Third Party collaborator under the ISIS Core Technology Patent Rights, the ISIS Formulation Patent Rights, the Manufacturing Patent Rights, the Research Target Patent Rights and the Third Party Patent Rights solely for the purpose of making, developing or using a Collaboration Compound or making, having made, using, developing, offering for sale or selling a Collaboration Compound Product.

(C) In the event of a material default by any Sublicensee under an ATL Sublicense, ATL will inform ISIS and take commercially reasonable efforts to cause the Sublicensee to cure the default or will terminate the ATL Sublicense. ATL will specifically state that ISIS is a third party beneficiary in any ATL Sublicense(s) hereunder.

4.4 Maximum Number of Licenses.

Not more than [***] Licenses to Research or Licenses to Exploit (including such licenses with respect to CD49d) may be in existence at any time during the term of this Agreement. Each such license is to a discrete Research Target.

4.5 Right of First Refusal.

(a) During the term of this Agreement, if ATL is approached by a Third Party regarding, or elects to offer to a Third Party, the opportunity to collaborate on the development of a compound that modulates a Research Target other than IGF-1R, ATL will provide written notice of same to ISIS. Such notice will include information identical to that presented by ATL to a Third Party including, at a minimum, (i) information possessed and disclosable by ATL that supports the development of such a compound and is reasonably necessary for ISIS to assess the commercial potential of

such compound; and (ii) a proposal that ATL would be prepared to accept. Within [***] days of receipt of such notice, ISIS will provide written notice to ATL indicating whether it is interested in negotiating with ATL to obtain the rights to develop and commercialize such compound with ATL.

(b) If ISIS fails to respond to ATL's notification within [***] days or indicates that it is not interested in developing and commercializing such compound with ATL, ATL will thereafter be free to enter into discussions with one or more Third Parties regarding the development and commercialization of such compound.

(c) If ISIS timely indicates its interest in obtaining such rights to develop and commercialize such compound with ATL, the parties will negotiate in good faith the terms of a separate development and commercialization agreement, which terms will be commercially reasonable, including without limitation license fees, milestone payments, and royalties, during the period up to [***] days following receipt of ISIS' notice. If the parties are unable to execute such an agreement within such time period, despite good faith negotiations by each party, ATL will thereafter be free to develop and commercialize such compound with one or more Third Parties, provided that the terms offered to such Third Party include financial terms that are no more favorable than those offered to ISIS.

(d) Notwithstanding the foregoing, this Section 4.5 will not apply to the Teva Sublicense.

4.6 Rights Retained by ISIS.

ISIS will retain the right to practice under all patent rights licensed to ATL hereunder as necessary to carry out ISIS' obligations under this Agreement and the Teva/ISIS Agreements, and for any purpose other than Exploiting the Collaboration Compound Products, except as provided otherwise herein. ATL will not practice any of the patent rights licensed to ATL hereunder other than as expressly licensed in this Article 4.

4.7 Access to Additional Technology.

(a) If, after the Effective Date and during the Collaboration Term, ISIS comes to own, or acquires a license with the right to grant sublicenses thereunder, any new or additional ISIS Core Technology Patent Rights or Manufacturing Patent Rights, and ATL desires access to such rights, ISIS agrees to negotiate in good faith with ATL regarding such access, provided that any licenses or sublicenses from ISIS to ATL under such Patents pursuant to Sections 4.1 and 4.2 are conditioned on ATL's agreement (i) to pay, on a flow-through basis, any royalties, milestones or other financial obligations owed to ISIS'

licensor arising from a license or sublicense grant to ATL and the practice under such license or sublicense by ATL, its Affiliates or Sublicensees; and (ii) to abide by all terms of the agreement under which a Third Party license is granted to ISIS.

(b) If, after the Effective Date and during the Collaboration Term, a change in the manufacturing process as a result of a change in the master batch records for ATL 1102 requires access of ATL to Manufacturing Patent Rights that were not practiced in the manufacture of the ATL 1102 API prior to such change, and if ISIS has obtained ownership or control of such Manufacturing Patent Rights by way of a license from or via collaboration with a Third Party, then any license or sublicense granted to ATL under such Manufacturing Patent Rights is conditioned on the prior agreement to be negotiated in good faith by the parties regarding (i) the assumption by ATL of all financial obligations owed to such Third Party arising from the grant of a license or sublicense to ATL and the practice under such license or sublicense by ATL, its Affiliates or Sublicensees; (ii) the payment to ISIS of an equitable portion of acquisition costs incurred by ISIS; and (iii) an agreement by ATL to abide by all terms of the agreement under which such Manufacturing Patent Rights were acquired, if applicable.

4.8 Effect of Termination of Licenses to Research and Licenses to Exploit.

(a) Return of ISIS-Provided Information. Upon termination of any License to Research or License to Exploit applicable to a Collaboration Compound or Collaboration Compound Product (including, without limitation, ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products), ATL will promptly return to ISIS, at no cost to ISIS, all information and materials provided to ATL by ISIS relating to such Collaboration Compound or Collaboration Compound Product.

(b) Return of API. Upon termination of any License to Research or License to Exploit applicable to a Collaboration Compound or Collaboration Compound Product (including, without limitation, ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products), ATL will promptly, subject [***] to ISIS all quantities of such Collaboration Compound API provided by ISIS that have not been used.

(c) Assignment Back to ISIS of VLA4 Compound Patent Rights. Upon termination of the License to Exploit ATL 1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products, ATL will promptly assign to ISIS all of ATL's right, title and interest in and to the VLA4 Compound Patent Rights. In connection therewith, ATL agrees to promptly execute all assignment and other documents, testify and take all other actions reasonably necessary or appropriate to transfer, effect, confirm, perfect, record, preserve, protect and enforce ISIS' right, title and interest in the VLA4 Compound Patent Rights throughout the world, at the reasonable request and expense (to the extent of any out-of-pocket costs incurred by ATL) of ISIS.

(d) Transition Plan for Research Targets Other Than CD49d. If a License to Research or License to Exploit, other than any such license with respect to ATL 1102, VLA4 Compounds and Other VLA4 Compounds and VLA4 Products, is terminated for any reason, promptly upon any such termination, the parties will prepare a transition plan to

ensure the seamless transition of any clinical studies and distribution and sales activities relating to any Antisense Inhibitor, Collaboration Compound, and/or Collaboration Compound Product from ATL to ISIS. In addition, ATL will provide ISIS with any and all data relating to such

Antisense Inhibitor, Collaboration Compound, Product using ISIS Standard Chemistry and/or to any ISIS Patent Rights relating to any Research Target that are in ATL's possession or control.

(e) Independently-Generated Information. Upon termination of any License to Research or License to Exploit applicable to a Collaboration Compound or Collaboration Compound Product (including, without limitation, ATL1102, VLA4 Compound, Other VLA4 Compounds and VLA4 Products), ATL will promptly assign and transfer to ISIS all information and materials (including, without limitation, preclinical and clinical data, regulatory submissions and Patents) relating to such Collaboration Compound or Collaboration Compound Product that were independently generated by ATL or any of its Affiliates, contractors and Sublicensees (collectively, "**Independently-Generated Information**"), excluding any such information independently generated by a Sublicensee (including Teva) that ATL is prohibited from providing to ISIS. ATL will obtain the written agreement of each Sublicensee (including Teva) to comply with the provisions of this Section 4.8(e). With respect to Independently-Generated Information provided to ISIS in the event of termination of a License to Research or License to Exploit, ISIS will compensate ATL as follows:

(1) If such termination occurs before the [***] of the Collaboration Compound or Collaboration Compound Product to which such Independently-Generated Information relates, ISIS or its Sublicensees will pay to ATL [***] using such Independently-Generated Information, for [***].

(2) If such termination occurs after the [***] of the Collaboration Compound or Collaboration Compound Product to which such Independently-Generated Information relates, ISIS or its Sublicensees will pay to ATL a [***] using such Independently-Generated Information, for [***].

(3) Any reasonable out-of-pocket costs payable by ATL to Third Parties (excluding any Sublicensee or any further sublicensee of a Sublicensee) associated with the physical transfer of Independently-Generated Information to ISIS pursuant to this Section 4.8(e) (*e.g.*, copying, shipping) will be borne by ISIS.

ARTICLE 5

ROYALTIES AND PAYMENTS

5.1 Minimum Royalties Payable to ISIS by ATL on Sales of Products by ATL or its Affiliates.

Subject to the terms and conditions of, and during the term of, this Agreement, ATL will pay to ISIS royalties on sales of Products by ATL or its Affiliates, according to the terms set forth below.

(a) The minimum royalty payable to ISIS by ATL for sales of any VLA4 Product by ATL or its Affiliates is [***] of Net Sales for as long as there are issued and unexpired claims within the patent rights applicable to such VLA4 Product (including, without limitation, the VLA4 Compound Patent Rights) and [***] of Net Sales thereafter for the life of such VLA4 Product.

(b) There is [***]for sales of any Product that contains a compound that modulates IGF-1R[***].

(c) Except as otherwise provided above, the minimum royalty payable to ISIS for sales of any Product by ATL or its Affiliates comprising a compound that modulates a Research Target or Abandoned Research Target for which ISIS has not established efficacy in an animal model and has not conducted preclinical toxicology studies is [***] of Net Sales. Such minimum royalty is due and payable for the life of the Product.

(d) Except as otherwise provided above, the minimum royalty payable to ISIS by ATL for sales of any Product by ATL or its Affiliates for which ISIS has established efficacy in an animal model or has conducted preclinical toxicity studies will be negotiated in good faith by the parties on a case-by-case basis, but will not be less than [***] of Net Sales.

(e) For Products under (a) or (c), in addition to any minimum royalties due under (a) or (c), the royalty payable to ISIS by ATL for sales of any Product by ATL or its Affiliates, the manufacture, use, sale, or importation of which would, but for the licenses granted hereunder, infringe an issued and unexpired claim under the ISIS Formulation Patent Rights is [***]

(f) The minimum royalties payable as described in Sections 5.1 (a)-(e) are in addition to any royalties payable to ISIS for Third Party Patent Rights as set forth in Section 5.3 below.

5.2 Sublicense Income Payable to ISIS by ATL or its Affiliates on Products sold by Sublicensee(s).

Subject to the terms and conditions of, and during the term of, this Agreement, ATL or its Affiliates will pay to ISIS certain shares of Sublicense Income received by ATL or its Affiliates, according to the terms set forth hereinbelow.

(a) The share of Sublicense Income payable to ISIS by ATL or its Affiliates on Sublicensee sales of a VLA4 Product is [***]

(b) [***].

(c) Except for VLA4 Products and products containing a compound that modulates IGF-1R, ATL will pay ISIS a [***] royalty on Net Sales of any Product by Sublicensee and [***] of Sublicense Income exclusive of royalties. Such amounts are due and payable for the life of the Product.

(d) In addition to amounts payable under (a) or (c), ATL will pay ISIS [***] of Sublicense Income for sales of Products by Sublicensees containing compounds that modulate a

Research Target other than IGF-1R and that that would, but for the licenses granted hereunder, infringe the ISIS Formulation Patent Rights. Such amounts are due and payable for the term of issued and unexpired claims within the ISIS Formulation Patent Rights.

(e) Except as otherwise provided above, the share of Sublicense Income payable to ISIS by ATL or its Affiliates for the license of rights to and/or sale of a Product for which ISIS has established efficacy in an animal model or has conducted preclinical studies will be negotiated in good faith by the parties, but will not be less than [***] of the Sublicense Income.

5.3 Royalties payable to ISIS for Third Party Patent Rights.

(a) In addition to the royalties and other payments set forth in Sections 5.1 and 5.2, as of the Amendment Date, the following royalties (percentages of Net Sales) are payable to ISIS by ATL for sales of Products (including Products that modulate IGF-1R), whether sold by ATL, its Affiliates, or Sublicensees, the manufacture, use, sale, or import of which would, but for the licenses granted hereunder, infringe an issued and unexpired claim of the following patent rights on a Product by Product basis:

[***]

(b) In addition to (a), for Collaboration Compound Products, including those that modulate IGF-1R, the manufacture, use, sale, or importation of which would, but for the licenses granted hereunder, [***].

(c) [***] Third Party Royalty Obligations. If, after the Amendment Date during the Collaboration Term, ISIS is successful in eliminating or reducing the requirement to pay a royalty under the Third Party license under which ISIS has obtained access to the [***], ISIS will so notify ATL. Thereafter, the royalty rate payable by ATL hereunder for the [***] will be [***]

5.4 Royalty Cap.

(a) Should the royalty payable by ATL to ISIS pursuant to Sections 5.1 and 5.3 with respect to sales of a VLA4 Product exceed [***] of Net Sales, the total royalty ATL must pay ISIS for such VLA4 Product will be [***] of Net Sales.

(b) Should the royalty payable by ATL to ISIS pursuant to Sections 5.1 and 5.3 with respect to sales of a Product other than a Product comprising a CD49d-modulating compound, exceed [***] of Net Sales, the total royalty ATL must pay ISIS for such Product will be [***] of Net Sales.

(c) The foregoing royalty caps apply only to the royalty rates set forth in Sections 5.1 and 5.3 and thus do not apply to any new technology or patent rights acquired or accessed by ISIS after the Effective Date, as described in Sections 4.7 and 8.4 or to the royalties owed pursuant to Section 5.2.

5.5 Examples.

(a) Example of Calculation of Royalty Rate for Sales of VLA4 Products by ATL or its Affiliates:

The royalty payable to ISIS for sales of VLA4 Product by ATL or its Affiliates (as a percentage of Net Sales) comprising non-topically-administered formulations of ATL 1102 is calculated as follows (assuming all relevant patent rights are issued and unexpired):

[***]

(b) Example of Royalties and Sublicense Income Payable to ISIS by ATL or its Affiliates on Sales of VLA4 Products by Sublicensees:

[***]

5.6 Payment of Royalties and Income; Reports.

ATL will make royalty payments to ISIS for each Product sold during a Calendar Quarter within [***] days after the last day of that Calendar Quarter. Each royalty payment will be preceded by a written report for that Calendar Quarter showing the calculation of Net Sales of the Product sold by ATL, its Affiliates and its Sublicensees worldwide during the quarterly reporting period and the calculation of the royalties and Sublicense Income payable under this Agreement, all on a country-by-country and Product-by-Product basis, which report will be delivered within 15 days of the last day of that Calendar Quarter.

5.7 Payment Modalities; Foreign Currency Conversion; Late Payment Charges.

(a) Payments. All payments to ISIS under this Agreement will be made in United States Dollars by bank wire transfer in next day available funds to such bank account in the United States designated in writing by ISIS from time to time. All amounts payable to ISIS hereunder are noncreditable and nonrefundable.

(b) Late Payments; Collections. In the event that any payment, including royalty, milestone or research payments, due hereunder is not made when due, the payment will bear interest from the date due at the lesser of (i) [***] per month, compounded monthly, or (ii) the highest rate permitted by law; provided, however, that in no event will such rate exceed the maximum legal annual interest rate. If ATL disputes the amount of an invoice presented by ISIS within [***] days of receipt of such invoice, the late fees will only apply to the correct amount as later determined or agreed. The payment of such interest will not limit a party from exercising any other rights it may have as a consequence of the lateness of any payment. In addition, ATL agrees to pay all costs of collection, including reasonable attorneys' fees, incurred by ISIS in enforcing the payment obligations of ATL after a due date has passed under this Agreement.

(c) Currency Conversion. Net Sales outside the United States will first be determined in the currency of the country in which they are earned and must then be converted into an

amount in United States dollars based on the average relevant rate of exchange throughout the then Calendar Quarter as reported in the *Wall Street Journal* (or if the *Wall Street Journal* ceases to be published, a comparable alternate publication agreed by the Parties).

5.8 Audits Requested by ISIS.

(a) Upon the written request of ISIS, and not more than once in each calendar year, ATL will permit ISIS' independent certified public accountant to have access during normal business hours to such of the records of ATL as may be reasonably necessary to verify the accuracy of the royalty reports hereunder for the current year and the preceding 2 years prior to the date of such request. The accounting firm will disclose to ISIS only whether the royalty reports are correct or incorrect, the specific details concerning any discrepancies, and the corrected amount of Net Sales and Sublicense Income. No other information will be provided to ISIS.

(b) At the request of ISIS, ATL will direct its Affiliates to permit audits of the Affiliates' records in accordance with the provisions of subsection (a) above. Further, ATL will include in each sublicense granted by it pursuant to this Agreement a provision requiring the Sublicensee to submit reports to ATL, to keep and maintain records of sales made pursuant to such sublicense and to grant access to such records by ISIS' independent accounting firm, to the same extent required of ATL hereunder. ISIS' independent accounting firm will also be granted access to such reports in ATL's possession as part of the audit referenced in subsection (a) above.

(c) If such accounting firm concludes that additional royalties were owed during such period, ATL will pay the additional royalties within [***] days of the date ISIS delivers to ATL such accounting firm's written report. The fees charged by such accounting firm will be paid by ISIS unless the additional royalties, milestones or other payments owed by ATL exceed [***] of the royalties, milestones or other payments paid for the time period subject to the audit, in which case ATL will pay the reasonable fees and expenses charged by the accounting firm.

(d) ISIS will treat all financial information subject to review under this Section 5.8 or under any sublicense agreement in accordance with the confidentiality provisions of Article 9, and will cause its accounting firm to enter into an acceptable confidentiality agreement with ATL and its Sublicensees obligating such firm to retain all such financial information in confidence pursuant to such confidentiality agreement.

5.9 Audits Requested by ATL.

(a) Upon the written request of ATL, and not more than once in each calendar year, ISIS will permit ATL's independent certified public accountant to have access during normal business hours to such of the records of ISIS as may be reasonably necessary to verify the accuracy of the invoices submitted to ATL hereunder for the 12 months preceding the date of such request. The accounting firm will disclose to ATL only whether the invoiced amounts are correct or incorrect, the specific details concerning the basis for the

invoiced amounts, and the corrected amount, if applicable. No other information will be provided to ATL.

(b) If such accounting firm concludes that any amounts invoiced were in error during such period and ATL is entitled to a refund of such amounts, ISIS will refund to ATL the amounts overcharged within [***] days of the date ATL delivers to ISIS such accounting firm's written report. The fees charged by such accounting firm will be paid by ATL unless the additional refunded amounts owed by ISIS exceed [***] of the total amount for which ATL was invoiced during the time period subject to the audit, in which case ISIS will pay the reasonable fees and expenses charged by the accounting firm.

(c) ATL will treat all financial information subject to review under this Section 5.9 in accordance with the confidentiality provisions of Article 9 and will cause its accounting firm to enter into an acceptable confidentiality agreement with ISIS obligating such firm to retain all such financial information in confidence pursuant to such confidentiality agreement.

5.10 Taxes.

If laws, rules or regulations require withholding of income taxes or other taxes imposed upon payments set forth in this Article 5, ATL will make such withholding payments as required and subtract such withholding payments from the payments set forth in this Article 5. ATL will submit appropriate proof of payment of the withholding taxes to ISIS within a reasonable period of time.

ARTICLE 6

USE OF MATERIALS, DATA AND INFORMATION

6.1 Unless provided otherwise herein, all Antisense Inhibitors and any related research materials delivered to ATL under this Agreement will be used only in furtherance of a Development Program or Collaborative Research Program, will not be used or delivered to or for the benefit of any Third Party (other than Teva) without the prior written consent of ISIS, and will not be used in research or testing involving human subjects. The Antisense Inhibitors and any related research materials supplied under this Agreement must be used with prudence and appropriate caution in any experimental work, since not all of their characteristics may be known. ATL agrees to comply with all applicable laws, rules and regulations in connection with its use of Antisense Inhibitors and related research materials provided hereunder.

6.2 All Antisense Inhibitors and related research materials provided to ATL hereunder are proprietary to ISIS.

6.3 ATL may use data and information provided to ATL by ISIS hereunder for internal drug discovery purposes only, consistent with the terms of this Agreement. Except as provided otherwise herein, all data and information provided to ATL by ISIS pursuant to

this Agreement is confidential and proprietary to ISIS and will not be disclosed to Third Parties, consistent with the provisions of Article 9 herein. ISIS acknowledges that ATL may wish to provide such data and/or information to a Third Party in connection with ATL's bona fide development, commercialization or partnering activities under this Agreement; ISIS will not unreasonably withhold its consent to such a transfer of data and information, provided that the receiving party is advised of the confidentiality provisions hereunder and agrees to be bound thereby. Notwithstanding the foregoing, ISIS reserves the absolute right to withhold consent if ATL wishes to transfer such data or information to an antisense company or other competitor of ISIS.

6.4 Notwithstanding Section 6.3, ISIS acknowledges and agrees that ATL may disclose to TEVA any data, information and know-how provided to ATL by ISIS under this Agreement that are relevant to ATL1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products without any requirement to obtain the further consent of ISIS, provided that all such data, information and know-how will remain subject to the provisions of this Article 6 and Article 9 hereof.

6.5 Consistent with the foregoing provisions, if ATL conducts studies comparing ISIS Standard Chemistry with the chemistry of a Third Party, all data and information incorporating or relating to ISIS Standard Chemistry that result from such studies is confidential and proprietary to ISIS and will not be disclosed to Third Parties, consistent with the provisions of Article 9 herein.

ARTICLE 7

FUNDING PROVISIONS

7.1 Funding for Development Activities.

(a) ATL will pay for all development activities that ISIS performs on ATL's behalf [***] including any such development activities with respect to VLA4 Compounds and Other VLA4 Compounds (except to the extent Teva is obligated to pay for such activities under the Teva/ISIS Agreements) and any such development activities described in any Development Plan hereunder or approved by the JDC in the course of any Development Program. Labor will be billed [***]. Materials and out of pocket expenses incurred by ISIS will be passed through to ATL at cost.

(b) ISIS will submit an invoice for such expenditures to ATL after each Calendar Quarter, and ATL will submit payment to ISIS within [***] days from the date of invoice, consistent with the provisions of Section 5.7.

7.2 Funding for Collaborative Research Program Activities.

(a) Except as specifically provided otherwise herein, as of the Effective Date, ATL will pay for all activities performed by ISIS in the course of the Collaborative Research Program hereunder [***]. Labor will [***]. Materials and out of pocket expenses incurred by ISIS will be [***]

(b) ISIS will submit an invoice for such expenditures to ATL after each Calendar Quarter, and ATL will submit payment to ISIS within [***] days from the date of invoice, consistent with the provisions of Section 5.7.

7.3 Funding for Other ATL Activities.

ATL will also pay for any other activities ATL deems necessary to research, develop or commercialize a Collaboration Compound or Product, or which are otherwise required for ATL to fulfill its obligations hereunder, [***]. Labor will [***]. Materials and out of pocket expenses incurred by ISIS will be [***].

ARTICLE 8

INTELLECTUAL PROPERTY

8.1 Ownership of Inventions.

(a) Neither party hereto will be deemed by this Agreement to have been granted any license or other rights to the other party's rights in any inventions, technology, discoveries, or other proprietary property (collectively, "Inventions"), except as expressly provided herein. Without limiting the generality of the foregoing, as between the parties, ISIS will at all times remain the sole and exclusive owner of the ISIS Patent Rights.

(b) Except as provided otherwise herein, each party will solely own all Inventions that are made (as determined by U.S. rules of inventorship) solely by employees of or Consultants to that party pursuant to the Collaborative Research Program or any Development Program under this Agreement. Such an Invention will be an "ISIS Invention" or an "ATL Invention," as the case may be, and Patents claiming such Inventions will be "ISIS Patents" or "ATL Patents," respectively.

(c) ISIS agrees to assign to ATL its rights in any ISIS Inventions or Joint Inventions claiming Antisense Inhibitors that modulate IGF-1R and methods of using same, provided that a License to Research or License to Exploit for IGF-1R exists. If ATL does not convert the License to Research for IGF-1R into a License to Exploit IGF-1R, or if the License to Research or License to Exploit applicable to IGF-1R is terminated for any reason, ATL will assign back to ISIS the latter's rights in any such ISIS Inventions and Joint Inventions, as well as ISIS' rights in any Patents filed on such Inventions. Notwithstanding the foregoing, if such assignment of rights back to ISIS would interfere with ATL's ability to practice any ATL Inventions or ATL Patent Rights pertaining to IGF-1R, ISIS agrees to sublicense, in favor of ATL, only that portion of any such Invention or Patent, and only for that time period, as is required for ATL to practice an ATL Invention or ATL Patent that would otherwise infringe the ISIS Invention or ISIS Patent, on a nonexclusive, mutually agreeable basis that is consistent with the royalties set out in this Agreement, provided that ISIS is not otherwise precluded from doing so.

(d) Except as provided otherwise herein, ISIS and ATL will jointly hold title to all Inventions, whether or not patentable, that are made (as determined by the U.S. rules of inventorship) jointly by employees of or Consultants to ISIS and ATL pursuant to the

Collaborative Research Program or any Development Program under this Agreement, as well as to Patents filed thereon. Such Inventions will be "Joint Inventions," and Patents claiming such Joint Inventions will be "Joint Patents." ISIS and ATL will promptly provide each other with notice whenever a Joint Invention is made. The parties agree and acknowledge that, except insofar as this Agreement provides otherwise, the default rights conferred on joint owners under US patent law, including the right of each party to independently practice, license and use a Joint Patent, will apply in relation to the Joint Patents throughout the world as though US patent law applied worldwide.

(e) The parties understand that if ATL or a Third Party collaborator of ATL provides a proprietary gene sequence or utility not known to ISIS, the discovery of inhibitors of that sequence may be a Joint Invention. Similarly, the parties understand that the discovery of a method of treating human disease by inhibiting a particular gene product, where ISIS' Antisense Inhibitor data is used to support the claims of the Patent, may be a Joint Invention.

(f) The parties agree, upon reasonable request, to execute any documents reasonably necessary to effect and perfect each other's ownership of any Invention.

8.2 Filing, Prosecution, Maintenance, Enforcement and Defense of Patents Owned or Controlled by ISIS and of Certain Joint Patents.

(a) Except as provided otherwise herein, ISIS will have the sole and exclusive right to file, prosecute, maintain, enforce and defend any Research Target Patent Rights and any ISIS Patents or Joint Patents filed on Inventions claiming an Antisense Inhibitor to a Research Target or a method of treatment using an antisense molecule that modulates a Research Target subject to a License to Research or License to Exploit hereunder, regardless of inventorship. ISIS will consider ATL's input with respect to the prosecution, maintenance, enforcement and defense of any such Patents. ISIS will also consider any supporting information provided by ATL that relates to the Research Target and its uses, as well as any supporting *in vivo* or *in vitro* efficacy data generated from experiments performed by ATL or its collaborators. As used herein, Patent prosecution includes, without limitation, the handling of interference proceedings, oppositions, reexaminations and reissues.

(b) In the event ATL proposes the filing of a Joint Patent pursuant to subsection (a) and ISIS does not wish to file and prosecute such Joint Patent, ATL will have the right to file, prosecute, maintain, enforce and defend such Joint Patent. ATL will consider ISIS' input with respect to the prosecution, maintenance, enforcement and defense of any such Joint Patents.

(c) ISIS will also have the sole and exclusive right, in its sole discretion, to file, prosecute, maintain, enforce and defend any Patents within the ISIS Core Technology Patent Rights, the Manufacturing Patent Rights, and the ISIS Formulation Patent Rights.

(d) ISIS will pay for its own labor costs incurred in the filing, prosecution, maintenance, enforcement and defense of any Patents for which ISIS is responsible hereunder.

(e) ATL will reimburse ISIS for reasonable materials and out of pocket expenses incurred in connection with the activities recited in subsections (a), (c) and (d). As used herein, materials and out of pocket expenses means costs, other than ISIS' labor costs, [***]. ISIS will invoice ATL on a quarterly basis and ATL will submit payment to ISIS consistent with the provisions of Article 7 herein.

(f) Should ATL elect not to pay expenses relating to Patent protection in a particular country, ATL will provide ISIS with written notice of same, and ATL's payment obligations with respect to that country will cease once ISIS has received such notice, provided that all noncancelable costs and expenses incurred by ISIS prior to such date will nevertheless be reimbursed by ATL. Immediately upon ISIS' receipt of such written notice from ATL, the applicable License to Research or License to Exploit will be terminated with respect to such country.

(g) With respect to any ISIS Patent Rights exclusively licensed to ATL under a License to Exploit, ISIS will promptly advise ATL if ISIS becomes aware of any suspected or actual infringement of such ISIS Patent Rights by any person. Similarly, ATL will promptly advise ISIS if ATL becomes aware of any suspected or actual infringement of such ISIS Patent Rights by any person.

(h) If ISIS fails to initiate proceedings against any actual or suspected infringement of the ISIS Patent Rights where such infringing activity involves an Antisense Inhibitor of a Research Target that ATL has a License to Exploit, or to defend any claim of infringement against the parties pertaining to such rights, within [***] days of receipt of a notice from ATL asking ISIS to do so, ATL will be entitled to initiate those proceedings at ATL's expense.

(i) Except as provided otherwise herein, ISIS will endeavor to take all action necessary to ensure that the ISIS Patent Rights that are or become subject to a License to Research or License to Exploit are maintained and diligently prosecuted.

8.3 Filing, Prosecution, Maintenance, Enforcement and Defense of Patents Owned or Controlled by ATL.

(a) ATL will have the sole and exclusive right and responsibility, in its sole discretion, to file, prosecute, maintain, enforce and defend (including the exclusive right to sue and exclude others from infringing) any Patents filed on Inventions made solely by ATL (i.e., ATL Patents) and VLA4 Compound Patent Rights. ATL will provide ISIS with a semiannual report summarizing the status of any such ATL Patents and VLA4 Compound Patent Rights. ATL hereby grants ISIS a worldwide, royalty-free, sublicensable, perpetual, nonexclusive license to practice under ATL's rights to any such ATL Patents and VLA4 Compound Patent Rights to carry out the activities contemplated by this Agreement and to make, have made, use, import, offer for sale and sell products other than a Product, provided that ATL is not contractually prohibited from doing so. If ATL decides to discontinue the maintenance, enforcement or defense of any such patent entirely, or in a particular country, it will notify ISIS in writing of that decision in sufficient time for ISIS to assume those responsibilities with respect to the relevant

patents (at ISIS' sole option), and will, on request by ISIS, transfer the relevant patent files to ISIS or a third party nominated by ISIS. ATL agrees not to narrow the scope of any existing VLA4 Compound Patent Rights unless agreed with ISIS in writing.

(b) If a License to Exploit is granted to ATL with respect to a Research Target or Collaboration Compound hereunder, ISIS will promptly thereafter transfer to ATL the sole and exclusive right to file, prosecute, maintain, enforce and defend any Patents owned, controlled by ISIS or to which ISIS has prosecution rights that are within the Research Target Patent Rights. ATL will consider ISIS' input with respect to the prosecution, maintenance, enforcement and defense of any such Patents. If ATL decides to discontinue the filing, prosecution, maintenance, enforcement or defense of any such Patent entirely or in a particular country, it will inform ISIS thereof with sufficient time for ISIS to assume those responsibilities with respect to such Patent and will thereafter transfer the relevant Patent files to ISIS or its designee.

8.4 Infringement of Third Party Patents.

If either party receives notice that a Product infringes a Third Party Patent, and the parties hereto agree to settle with and pay royalties to such Third Party, the additional royalty burden will be allocated as follows.

(a) If the alleged infringement is due to ATL's practice of ISIS Core Technology Patent Rights, Manufacturing Patent Rights, or VLA4 Compound Patent Rights, [***].

(b) If the alleged infringement is due to ATL's practice of any other Patent Rights licensed hereunder, [***].

8.5 Patent Coordinators.

(a) Within 30 days of the Effective Date, the parties will each select a Patent Coordinator ("PC") to facilitate and coordinate the preparation, filing, prosecution and maintenance of Patents pursuant to this Agreement. The parties may agree to name additional Patent Coordinators, as long as equal representation is maintained.

(b) During the Collaboration Term, the PCs will be the primary contacts for interaction between the parties with respect to the activities referenced in (a).

(c) The PCs will meet as needed during the Collaboration Term. Meetings will be via teleconference or videoconference, or as the parties may otherwise agree. The frequency, dates and times of all meetings will be mutually agreed upon by the parties. At their first meeting, the PCs will determine such procedures as they will reasonably require to conduct their activities.

(d) The parties further agree that to facilitate the activities described in this Section, ATL's Patent Coordinator may, upon prior written notice to ISIS' Patent Coordinator and at such times as are mutually agreed upon by the Patent Coordinators, obtain access to and make copies of Patent file documents that are relevant to filing, prosecution, maintenance, enforcement and defense of Patents licensed to ATL hereunder. Any and all such documents will be maintained by ATL in confidence, pursuant to the provisions of Article 9 below.

ARTICLE 9

CONFIDENTIALITY

9.1 Nondisclosure Obligation.

All Confidential Information disclosed by one party to the other party hereunder will be maintained in confidence by the receiving party and will not be disclosed to a Third Party or Affiliate or used for any purpose except as set forth below.

9.2 Permitted Disclosures.

Except as otherwise provided herein, a party may disclose Confidential Information received from the other party:

(a) to governmental or other regulatory agencies in order to obtain Patents or approval to conduct clinical trials, or to gain Marketing Approval; provided that such disclosure may be made only to the extent reasonably necessary to obtain such patents or approvals;

(b) to Affiliates, Sublicensees (including Teva), agents, consultants, and/or other Third Parties to allow the Exploitation of Products (or for such parties to determine their interest in performing such activities) in accordance with this Agreement on the condition that such Affiliates and Third Parties agree to be bound by confidentiality obligations no less stringent than those contained in this Agreement, provided the term of confidentiality for such Affiliates and Third Parties will be no less than 7 years; or

(c) if such disclosure is required by law or court order, provided that notice is promptly delivered to the other party in order to provide an opportunity to challenge or limit the disclosure obligations.

ARTICLE 10

PUBLICATION AND PUBLICITY

10.1 Publication.

(a) The parties agree that it is customary in the industry to publish results obtained from clinical trials and other studies of a Collaboration Compound or Product, and that each party may publish such information obtained by such party in the performance of the Development Program, subject to the provisions of this Section.

(b) Except as provided otherwise herein, the parties will be entitled to publish or present on the results of any Development Program or other development activities hereunder, including, without limitation, the development of any ATL1102, VLA4 Compound, Other VLA4 Compound or other Collaboration Compound, or any Product, provided that

the party seeking to publish will deliver to the other party for its review a copy of any proposed publication or an abstract of any oral presentation of clinical results at scientific meetings involving any ATL1102, VLA4 Compound or Other VLA4 Compound or other Collaboration Compound, or any Product hereunder, or the Proprietary Information of the other party, at least 30 days prior to submission of scientific publications or abstracts of oral presentations. The reviewing party will have the absolute right to request that any of its Proprietary Information be deleted from such publication or presentation, and the disclosing party will comply with that request. If the disclosing party does not receive any feedback from the reviewing party within that 30-day period, the disclosing party will be free to proceed with the publication or presentation, with the following limitations:

(i) ISIS will be permitted to publish on matters relating to ATL1102 or any VLA4 Compound or Other VLA4 Compound or other Collaboration Compound, or any Product developed by ATL hereunder during the term of this Agreement only upon the prior written approval of ATL, which may be reasonably withheld by ATL.

(ii) ATL will be permitted to publish on matters relating to any Manufacturing Technology or Manufacturing Technology Improvements relating to a specific Collaboration Compound or Product developed hereunder during the term of this Agreement only upon the prior written approval of ISIS, which may be given at ISIS' sole discretion.

(c) For the avoidance of doubt, the provisions of this Section 10.1 will apply to Sublicensees (including Teva) to the same extent as they apply to ATL.

(d) Notwithstanding anything in this Section 10 ISIS acknowledges and agrees that, other than in respect of the ATL1102 Phase IIa Trial, ISIS does not have the right to publish information obtained in the performance of development activities conducted by or on behalf of Teva relating to ATL1102, VLA4 Compounds and Other VLA4 Compounds.

10.2 Publicity.

(a) The parties will issue a joint press release regarding the execution of this Agreement.

(b) Except as otherwise provided herein or required by law, neither party will originate any publication, news release or other public announcement, written or oral, whether in the public press, or stockholders' reports, or otherwise, relating to this Agreement, and neither party will use the name, trademark, trade name, logo or likeness of the other party or its employees in any publicity, news release or disclosure relating to this Agreement, or its subject matter, without the prior express written permission of the other party.

(c) ATL will inform ISIS of any press releases relating to a Product permitted hereunder or required to be made by law in advance of general release to the public.

(d) For the avoidance of doubt, the provisions of this Section 10.2 will apply to Sublicensees (including Teva) to the same extent as they apply to ATL.

ARTICLE 11

INDEMNIFICATION

11.1 Indemnification by ATL.

ATL will indemnify, defend and hold ISIS and its agents, employees, officers and directors (the "ISIS Indemnitees") harmless from and against any and all liability, damage, loss, cost or expense (including reasonable attorneys' fees) arising out of Third Party claims or suits related to (a) ATL's performance of its obligations under this Agreement; (b) breach by ATL of its representations and warranties set forth in Article 13; (c) patent infringement allegations or claims asserted by a Third Party against ISIS arising out of ISIS' performance of activities for ATL pursuant to this Agreement; (d) ATL's choice of Research Targets pursuant to Section 3.4 or 3.5; or (e) the development, manufacture, use, handling, storage, sale or other disposition of any Collaboration Compound or Product by ATL or any of its Affiliates, contractors or Sublicensees (including Teva); *provided, however*, that ATL's obligations pursuant to this Section 11.1 will not apply to the extent such claims or suits result from the gross negligence or willful misconduct of any of the ISIS Indemnitees. Notwithstanding the foregoing, ATL will have no obligation to indemnify the ISIS Indemnitees with respect to claims arising out of breach by ISIS of its representations and warranties set forth in Section 13.1.

11.2 Indemnification by ISIS.

ISIS will indemnify, defend and hold ATL and its Affiliates and each of their respective agents, employees, officers and directors (the "ATL Indemnitees") harmless from and against any and all liability, damage, loss, cost or expense (including reasonable attorney's fees) arising out of Third Party claims or suits related to (a) ISIS' performance of its obligations under this Agreement; or (b) breach by ISIS of its representations and warranties set forth in Article 13; *provided however*, that ISIS' obligations pursuant to this Section 11.2 will not apply to the extent that such claims or suits result from the gross negligence or willful misconduct of any of the ATL Indemnitees. Notwithstanding the foregoing, ISIS will have no obligation to indemnify the ATL Indemnitees with

respect to claims arising out of (i) a breach by ATL of its representations and warranties set forth in Sections 3.5(b)(i) and 13.1, or (ii) ISIS' performance of development or other activities with respect to ATL 1102 on behalf of ATL or Teva in accordance with ATL's or Teva's instructions or specifications.

11.3 Notification of Claims; Conditions to Indemnification Obligations.

As a condition to a party's right to receive indemnification under this Article 11, it will (i) promptly notify the other party as soon as it becomes aware of a claim or action for which indemnification may be sought pursuant hereto, (ii) cooperate with the indemnifying party in the defense of such claim or suit, and (iii) permit the indemnifying party to control the defense of such claim or suit, including without limitation the right to select defense counsel. In no event, however, may the indemnifying party compromise or settle any claim or suit in a manner which admits fault or negligence on the part of the indemnified party without the prior written consent of the indemnified party. The indemnifying party will have no liability under this Article 11 with respect to claims or suits settled or compromised without its prior written consent.

ARTICLE 12

TERM AND TERMINATION OF AGREEMENT

12.1 Term and Termination of Agreement.

This Agreement will be effective as of the Effective Date and unless terminated earlier pursuant to Sections 12.2 below, the term of this Agreement will continue in effect until expiration of the License Term.

12.2 Termination upon Fundamental Breach.

(a) General. Subject to subsections (b) and (c) below, this Agreement may be terminated upon written notice by either party to the other at any time during the term of this Agreement if the other party is in fundamental breach of its obligations hereunder (i.e., a breach which goes to the heart of the Agreement) and has not cured such breach within 90 days after written notice requesting cure of the breach; providing, however, that in the event of a good faith dispute with respect to the existence of such a fundamental breach, the 90-day cure period will be stayed until such time as the dispute is resolved pursuant to Section 16.6 hereof. Material breaches that are not fundamental give rise solely to a right of damages but not a right to terminate the Agreement.

(b) Fundamental Breach by ATL.

(i) Relating to CD49d. If ATL commits a fundamental breach of this Agreement that relates to CD49d, ATL 1102 or any VLA4 Compounds, Other VLA4 Compounds or VLA4 Product for which ISIS provides written notice under Section 12.2(a), ISIS will concurrently provide a copy of such notice to Teva in accordance with the notice provisions of the Teva/ISIS Agreements, and Teva will have the right to cure such breach on ATL's behalf.

(ii) Not Relating to CD49d. Notwithstanding the provisions of Section 12.2(a), if ATL commits a fundamental breach of this Agreement unrelated to CD49d, ATL 1102 or any VLA4 Compounds, Other VLA4 Compounds or VLA4 Product for which ISIS provides written notice under Section 12.2(a), ISIS will concurrently provide a copy of such notice to Teva in accordance with the notice provisions of the Teva/ISIS Agreements, and if such breach is not timely cured in accordance with Section 12.2(a), this Agreement will: (A) terminate as it relates to Research Targets other than CD49d, ATL1102 and Collaboration Compounds other than VLA4 Compounds and Other VLA4 Compounds; and (B) remain in full force and effect in accordance with its terms (including, without limitation, this Section 12.2) as it relates to CD49d, ATL 1102, VLA4 Compounds and Other VLA4 Compounds.

(c) Fundamental Breach by ISIS. If ISIS commits a fundamental breach of this Agreement for which ATL provides written notice under Section 12.2(a), and such breach is not timely cured in accordance with Section 12.2(a), ATL may, at its option, terminate this Agreement either: (i) in its entirety; or (ii) solely as it relates to Research Targets other than CD49d, ATL 1102 and Collaboration Compounds other than VLA4 Compounds and Other VLA4 Compounds, in which event this Agreement will remain in full force and effect in accordance with its terms (including, without limitation, this Section 12.2) as it relates to CD49d, ATL 1102, VLA4 Compounds and Other VLA4 Compounds. ATL's notice under Section 12.2(a) will specify which of the foregoing termination options ATL elects.

12.3 Rights in Bankruptcy.

All rights and licenses granted under or pursuant to this Agreement by ISIS or ATL are, and will otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of right to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The parties agree that the parties, as licensees of such rights under this Agreement, will retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code. The parties further agree that, in the event of the commencement of a bankruptcy proceeding-by or against either party under the U.S. Bankruptcy Code, the party hereto which is not a party to such proceeding will be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, and same, if not already in their possession, will be promptly delivered to them (i) upon any such commencement of a bankruptcy proceeding upon their written request therefor, unless the party subject to such proceeding elects to continue to perform all of its obligations under this Agreement, or (ii) if not delivered under (i) above, following the rejection of this Agreement by or on behalf of the party subject to such proceeding upon written request therefor by the non-subject party.

12.4 Accrued Rights and Surviving Obligations.

Expiration or termination of the Agreement will not relieve the parties of any obligation accruing prior to such expiration or termination. Sections 4.8, 12.4 and 16.7, and Articles 5-9, 11 and 13-15 will survive expiration or termination of the Agreement. Provisions concerning reporting requirements will continue

in effect in accordance with any applicable timetables set forth herein. Any expiration or early termination of this Agreement will be without prejudice to the rights of either party against the other accrued or accruing under this Agreement prior to termination, including the obligation to pay royalties for Product sold prior to such termination.

ARTICLE 13

REPRESENTATIONS AND WARRANTIES; DISCLAIMER

13.1 Representations and Warranties of the parties.

Each party represents and warrants to the other party that, as of the Amendment Date:

(a) Such party is duly organized and validly existing under the laws of the state of its incorporation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

(b) Such party has taken all corporate action necessary to authorize the execution and delivery of this Agreement and the performance its obligations under this Agreement;

(c) This Agreement is a legal and valid obligation of such party, binding upon such party and enforceable against such party in accordance with the terms of this Agreement The execution, delivery and performance of this Agreement by such party does not conflict with any agreement, instrument or understanding, oral or written, to which such party is a party or by which such party may be bound, and does not violate any law or regulation of any court, governmental body or administrative or other agency having authority over such party. All consents, approvals and authorizations from all governmental authorities or other Third Parties required to be obtained by such party in connection with this Agreement have been obtained;

(d) Such party has the full and exclusive right, power and authority to enter into this Agreement, to perform the Development Program, the Collaborative Research Program and to grant the licenses granted hereunder;

(e) There are no agreements between such party and any Third Parties which would preclude or otherwise limit such party's ability to conduct its tasks and obligations under the Development Plan, the Collaborative Research Program or otherwise fulfill its obligations under this Agreement; and

(f) All individuals who will perform any activities on such party's behalf in connection with the Development Program and/or the Collaborative Research Program have assigned to such party or its Affiliates the whole of their rights in any intellectual property conceived or reduced to practice by them as a result of either program.

13.2 Representations and Warranties by ATL.

ATL warrants and represents that to the best of its knowledge, none of the Research Targets listed on Exhibit 3.4 as of the Amendment Date are encumbered by any Third Party rights including, without limitation, intellectual property rights, that would interfere with ISIS' ability to carry out the activities contemplated by the parties hereunder. ATL further warrants and represents that, to the best of its knowledge as of the Amendment Date, if ISIS makes an Antisense Inhibitor to any of the Research Targets, it will not constitute an infringement of any Third Party rights and that ATL will indemnify ISIS, as set forth in Section 11.1 herein, should a subsequent determination be made that Third Party rights were infringed.

13.3 Representations and Warranties by ISIS.

ISIS warrants and represents that, to the best of its knowledge as of the Amendment Date, the practice of the technology claimed in the ISIS Core Technology Patent Rights and the Manufacturing Patent Rights will not infringe any Third Party patents.

ISIS further warrants and represents, as of the Amendment Date, that: (a) the VLA4 Compound Patent Rights set out in Exhibit 1.16(A) are enforceable, including that all assignments and maintenance fees have been timely filed and paid with respect to the VLA4 Compound Patent Rights; and (b) to the best of ISIS' knowledge as of the Amendment Date, without reference to a specific development plan and without any investigation, the ISIS Core Technology Patent Rights, ISIS Formulation Patent Rights, Manufacturing Patent Rights, Research Target Patent Rights and VLA4 Compound Patent Rights, considered together, constitute all of the Patents controlled by ISIS that are necessary for ATL to develop and commercialize ATL 1102, the VLA4 Compounds and Other VLA4 Compounds using the ISIS Standard Chemistry.

13.4 Disclaimers.

THE ANTISENSE INHIBITORS BEING PROVIDED TO ATL HEREUNDER ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

THE PARTIES EXPRESSLY DISCLAIM ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT OF THIRD PARTY RIGHTS, UNLESS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT.

ARTICLE 14

NOTICE

14.1 Notice.

All notices which are required or permitted hereunder will be in writing and sufficient if delivered personally, sent by facsimile (and promptly confirmed by personal delivery, registered or certified mail or overnight courier), sent by nationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, addressed as follows:

if to ISIS, to:	Isis Pharmaceuticals, Inc. 1896 Rutherford Road Carlsbad, CA 92008 USA Attention: Chief Operating Officer Fax No.:+1 (760) 931-9639
with a copy to:	Attention: General Counsel Fax No.:+1 (760) 268-4922

if to ATL, to:	Antisense Therapeutics, Limited ACN 095 060 745 of Level 1 10 Wallace Avenue, Toorak Victoria 3142, AUSTRALIA Attention: CEO Fax No.: +61 (3) 9826 4399
with a copy to:	Attention: General Counsel Fax No.: +61 (3) 9826 4399

or to such other address as the party to whom notice is to be given may have furnished to the other party in writing in accordance herewith. Any such notice will be deemed to have been given when delivered if personally delivered or sent by facsimile on a Business Day, on the Business Day after dispatch if sent by nationally-recognized overnight courier and on the third Business Day following the date of mailing if sent by mail.

ARTICLE 15

RECORDS

15.1 Records.

Each party will maintain records, in sufficient detail and in good scientific manner, which will fully and properly reflect all work done and results achieved in the development of any VLA4 Compounds, Other VLA4 Compounds or other Collaboration Compound, or any Product, hereunder and in the performance of its responsibilities under each Development Plan hereunder. Each party will have the right, during normal business hours and upon reasonable prior notice, to inspect and copy those records of the other party referred to herein that are necessary or useful to the inspecting party for the purposes of making any required filings with Regulatory Authorities in order to obtain manufacturing approvals and/or Marketing Approvals. Each party will maintain such records and the information disclosed therein in confidence in accordance with Article 9. ISIS acknowledges and agrees that ISIS' right of inspection under this clause 15.1 does not extend to allowing ISIS to inspect any records held by Teva under the Teva Sublicense.

ARTICLE 16

MISCELLANEOUS PROVISIONS

16.1 Relationship of the parties.

It is expressly agreed that ISIS and ATL will be independent contractors and that the relationship between the two parties will not constitute a partnership, joint venture or agency. Neither ISIS nor ATL will have the authority to make any statements, representations or commitments of any kind, or to take any action, which will be binding on the other, without the prior consent of the other party.

16.2 Successors and Assigns.

Neither this Agreement nor any interest hereunder may be assigned or otherwise transferred, nor, except as expressly provided hereunder, may any right or obligations hereunder be assigned or transferred by either party without the prior written consent of the other party; provided, however, that either party may, without such consent, assign the Agreement and its rights and obligations hereunder to an Affiliate or in connection with the transfer or sale of all or substantially all of its assets, or in the event of its merger or consolidation or change in control or similar transaction. Any permitted assignee will assume all obligations of its assignor under the Agreement, except that no intellectual property of any Third Party acquirer of ATL or ISIS will be included in the licenses granted hereunder. This Agreement will be binding upon the successors and permitted assigns of the parties. Any attempted assignment not in accordance with this Section 16.2 will be void.

16.3 Entire Agreement; Amendments.

This Agreement contains the entire understanding between ATL and ISIS with respect to the license, development and commercialization of antisense APIs hereunder. All express or implied agreements and understandings, either oral or written, heretofore made by ATL and ISIS on the same subject matter (including, without limitation, the Original Agreement) are expressly superseded by this Agreement. The Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by both parties hereto.

16.4 Force majeure.

Neither party will be held liable or responsible to the other party nor be deemed to have defaulted under or breached the Agreement for failure or delay in fulfilling or performing any term of the Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party including, without limitation, embargoes, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, or acts of God. The affected party will notify the other party of such force majeure circumstances as soon as reasonably practical and will make every reasonable effort to mitigate the effects of such force majeure circumstances.

16.5 Applicable law

The Agreement will be governed by and construed in accordance with the laws of the State of Delaware without reference to any rules of conflict of laws.

16.6 Dispute resolution

(a) The parties recognize that disputes may from time to time arise between the parties during the term of this Agreement. In the event of such a dispute, either party, by written notice to the other party, may have such dispute referred to the parties' respective executive officers designated below or their successors, for attempted resolution by good faith negotiations within 30 days after such notice is received. Said designated officers are as follows:

For ISIS:	Chief Operating Officer
For ATL:	CEO

(b) In the event the designated executive officers are not able to resolve such dispute after such 30-day period, each party may pursue its rights and remedies in law or equity in any court of competent jurisdiction.

16.7 No consequential damages

IN NO EVENT WILL EITHER PARTY OR ANY OF ITS RESPECTIVE AFFILIATES BE LIABLE TO THE OTHER PARTY OR ANY OF ITS AFFILIATES FOR SPECIAL, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, INCLUDING, BUT NOT LIMITED TO, LOSS OF PROFITS OR REVENUE, OR CLAIMS OF CUSTOMERS OF ANY OF THEM OR OTHER THIRD PARTIES FOR SUCH OR OTHER DAMAGES.

16.8 Third party beneficiary

The parties hereby acknowledge and agree that Teva is an intended third party beneficiary of this Agreement solely as it relates to CD49d, ATL1102, VLA4 Compounds, Other VLA4 Compounds and VLA4 Products.

16.9 Captions

The captions to the several Articles and Sections hereof are not a part of the Agreement, but are merely a convenience to assist in locating and reading the several Articles and Sections hereof.

16.10 Waiver

The waiver by either party hereto of any right hereunder, or the failure to perform, or a breach by the other party will not be deemed a waiver of any other right hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

16.11 Compliance with law

Nothing in this Agreement will be deemed to permit a party to export, re-export or otherwise transfer any Licensed Product sold under this Agreement without compliance with applicable laws.

16.12 Severability.

In the event any one or more of the provisions contained in this Agreement should be held invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein will not in any way be affected or impaired thereby, unless the absence of the invalidated provision(s) adversely affect the substantive rights of the parties. The parties will in such an instance use their best efforts to replace the invalid, illegal or unenforceable provision(s) with valid, legal and enforceable provision(s) which, insofar as practical, maintains the balance of the rights and obligations of the parties under this Agreement.

16.13 Waiver of Rule of Construction.

Each party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement will be construed against the drafting party will not apply.

16.14 Counterparts.

The Agreement may be executed in two or more counterparts, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the Amendment Date.

ANTISENSE THERAPEUTICS, LIMITED	**ISIS PHARMACEUTICALS, INC.**
By: /s/ Mark Diamond	By: /s/ B. Lynne Parshall
Name: Mark Diamond	Name: B. Lynne Parshall
Title: MD & CEO	Title: COO & CFO

CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R §§ 200.80(b)4, AND 240.24b-2

EXECUTION VERSION *(02/08/08)*

EXHIBIT 1

DEFINITIONS

1.1 "Abandoned Research Target" has the meaning set forth in Section 3.5(d) herein.

1.2 "Active Program" in relation to a Collaboration Compound or Product means an ongoing program for optimizing, developing and commercializing such Collaboration Compound or Product, including preclinical studies, human clinical studies, development activities aimed at obtaining registration for marketing, and marketing and selling activities. Except as set forth in Section 2.2(b), an Active Program includes the following specific **"Development Milestones"** that must be met in order for the Collaboration Compound or Product to achieve and maintain **"Active Development"** status:

(a) initiation of phenotypic or functional assays by ATL within 12 months of ATL's receipt of reasonably sufficient quantities of the Antisense Inhibitors directed to a Research Target and corresponding control oligonucleotides;

(b) initiation of IND-enabling toxicology studies by ATL within 18 months of ATL's receipt of an Antisense Inhibitor directed to a Research Target;

(c) filing of an IND not later than 6 months after the completion of IND-enabling studies;

(d) initiation of Phase I studies not later than 6 months after the filing of the IND;

(e) initiation of Phase IIa studies not later than 24 months after the initiation of Phase I studies;

(f) initiation of Phase III studies not later than 3 years after the initiation of Phase IIa studies;

(g) filing of an NDA not later than 18 months after the successful completion of a pivotal trial; and

(h) the use of commercially reasonable efforts by ATL to bring each Product to market and to maximize the commercial value of each such Product worldwide.

If ATL will not be able to meet a Development Milestone set forth above for [***], ATL will be granted a [***]month extension on any of the milestones identified in above, provided that ATL (i) gives the JDC members at least [***] months' prior written notice that it is [***], and (ii) demonstrates to the JDC that it has [***]. If the JDC cannot agree on this issue, the matter will be referred to the designated officers of ATL and ISIS for resolution, consistent with the provisions of Section 16.6(a).

Except as set forth in Section 2.2(b)(i) herein, a compound that is in "Active Development" is one that is in an Active Program, as defined above.

1.3 "Affiliate" with respect to any person, organization, corporation or other business entity (collectively, "Person"), means any other Person controlling, controlled by, or under common control with such Person. For purposes of this definition, "control" refers to the possession, directly or indirectly, of the power to direct the management or policies of a Person, whether through the ownership of voting securities, by contract or otherwise, of a Person.

1.4 **"Amendment Date"** has the meaning set forth in the first paragraph of this Agreement.

1.5 **"Antisense Inhibitor"** means an oligonucleotide or analog thereof that inhibits protein synthesis at the nucleic acid level by specifically binding to the sequence of a selected messenger or viral ribonucleic acid (RNA) by base-pairing, thus causing a selective inhibition of gene expression.

1.6 **"Antisense Technology"** means the selective modulation of protein synthesis at the nucleic acid level caused by the binding of an oligonucleotide or an analog thereof to a complementary sequence.

1.7 **"ATL 1102"** means the Antisense Inhibitor (also known as ISIS 107248) that inhibits production of CD49d and comprises the sequence claimed as [***] and ISIS Standard Chemistry as set forth in Exhibit 1.7.

1.8 **"ATL Invention"** has the meaning set forth in Section 8.1(b).

1.9 **"ATL Patent"** has the meaning set forth in Section 8.1(b).

1.10 **"ATL Sublicense"** has the meaning set forth in Section 4.3(b).

1.11 **"Australian Approval"** means approval of a Product for marketing in Australia by the Therapeutic Goods Administration ("TGA"), without the requirement for price having been approved. If a Product can be sold in Australia without TGA approval, Australian Approval will be deemed to have been obtained on the first sale of a Product in Australia.

1.12 **"Business Day"** means any calendar day, except that if an activity to be performed or an event to occur (including, without limitation, the receiving of a notice under Article 14 and other communications) falls on a Friday, Saturday, Sunday, or a recognized public or bank holiday (as determined in the place of performance of the applicable activity or occurrence of the applicable event), then the activity may be performed or the event may occur on the next day that is not a Saturday, Sunday, or a public or bank holiday.

1.13 **"Calendar Quarter"** means the respective periods of 3 consecutive calendar months ending on March 31, June 30, September 30 and December 31.

1.14 **"Calendar Year"** means each successive period of 12 months commencing on January 1 and ending on December 31.

1.15 **"Change of Control"** means the consummation, after the Amendment Date, of a transaction or a related series of transactions in which: (a) any Third Party becomes the beneficial owner, directly or indirectly, of more than 50% of the total voting power of ATL's or ISIS' (as applicable) stock then outstanding normally entitled to vote in elections of directors; (b) ATL or ISIS (as applicable) consolidates with or merges into a Third Party, or any Third Party consolidates with or merges into ATL or ISIS, in either event pursuant to a transaction in which more than 50% of the total voting power of the stock outstanding of the surviving entity normally entitled to vote in elections of directors is not held by Persons holding at least 50% of the outstanding voting stock of ATL or ISIS preceding such consolidation or merger; or (c) ATL or ISIS conveys, transfers or leases all or a substantial portion of its assets relating to ATL 1102, VLA4 Compounds, Other VLA4 Compounds or VLA4 Products to a Third Party.

1.16 **"CD49d"** means the target that is modulated by ATL 1102, which is known as CD49d and is a Research Target hereunder.

1.17 **"Collaboration"** has the meaning set forth in Section 2.1.

1.18 **"Collaboration Compound"** means an Antisense Inhibitor of a Research Target that is discovered or developed by ISIS that (i) incorporates Antisense Technology; (ii) incorporates ISIS Standard Chemistry; (iii) is subject to a License to Research or License to Exploit hereunder; and (iv) is in Active Development, consistent with Section 1.2 herein.

1.19 **"Collaboration Compound Product"** means a product containing a Collaboration Compound.

1.20 **"Collaboration Term"** means the term of the Collaborative Research Program as set forth in Section 3.1.

1.21 **"Collaborative Research Plan"** has the meaning set forth in Section 3.1, as further detailed in Exhibit 3.1.

1.22 **"Collaborative Research Program"** means the research program described in Article 3, as modified from time to time by the parties (e.g., via the JRC).

1.23 **"Confidential Information"** means information which is (a) of a confidential and proprietary nature; (b) designated by either party as Confidential Information or Proprietary Information; and (c) not readily available to that party's competitors and which, if known by a competitor of that party, might lessen any competitive advantage of that party or give such competitor a competitive advantage. Confidential Information which is disclosed in oral, written, graphic, electronic or any other form by one party to the other party that is clearly marked as "confidential" or "proprietary." Oral information must be reduced to writing and designated as "confidential" within 30 days of disclosure.

For the purposes of this Agreement, "Confidential Information" includes, without limitation, (a) information that is proprietary or confidential or which is treated by that party as confidential and which relates either directly or indirectly to the business of that party regardless of the form in which that information is constituted, and which is not lawfully in the public domain; and (b) any confidential information in relation to Patents, technology, know-how, or any improvements owned or controlled by a party hereto.

"Confidential Information" will not include any information that the receiving party can establish by written records:

(i) was known by it prior to the receipt of Confidential Information from the disclosing party;

(ii) was disclosed to the receiving party by a Third Party having the right to do so;

(iii) was, or subsequently became, in the public domain through no fault of the receiving party, its officers, directors, employees or agents;

(iv) was concurrently or subsequently developed by personnel of the receiving party without having had access to the disclosing party's Confidential Information;

(v) as disclosed with the prior written consent of the disclosing party; or

(vi) was disclosed by the receiving party pursuant to any judicial or governmental request, requirement or order, so long as the receiving party provides the disclosing party with sufficient prior notice in order to allow the disclosing party to contest such request, requirement or order.

1.24 **"Consultant"** means an individual who is not an employee of either party hereto, but who has been engaged by a party hereto in order to perform certain activities, wherein that individual has an obligation to assign to the engaging party, at the time an Invention is made, all rights that individual may have in such Invention.

1.25 **"[***] Targets"** means those Research Targets designated as [***] Targets, as listed in Section A of Exhibit 3.4.

1.26 **"Development Milestones"** means the Development Milestones set forth in Section 1.2 hereinabove.

1.27 **"Development Plan"** means the plan for the development of any Antisense Inhibitor or Collaboration Compound hereunder.

1.28 **"EC/EMEA Approval"** means approval of a Product for marketing in the European Commission (**EC**), or if ATL seeks approval through mutual recognition in the European Union, by the Ministry of Health of the United Kingdom, France, Germany, Italy or Spain (each a "Major European Country"), without the requirement for price having been approved. If a Product can be legally sold in a Major European Country without EC or Ministry of Health approval, EC/EMEA Approval will be deemed to have been obtained on the first sale of a Product in a Major European Country.

1.29 **"Effective Date"** has the meaning provided in the "Introduction and Overview" set forth on the first page of this Agreement.

1.30 **"Exploit"** means to research, develop, test, import, export, make, have made, use, market, manufacture, sell, offer for sale, register, record, have sold, sublicense, commercialize, distribute and otherwise exploit.

1.31 **[***]**.

1.32 **[***]**.

1.33 **"IND"** means an Investigational New Drug Application or similar application or submission for approval to conduct human clinical investigations filed with or submitted to a Regulatory Authority or hospital ethics committee in conformity with applicable Regulatory Authority regulations.

1.34 **"Independently-Generated Information"** has the meaning set forth in Section 4.8(e) herein.

1.35 **"IND-Enabling Studies"** means, at a minimum, the pharmacokinetic and toxicology studies required to meet the safety regulations for filing an IND, as well as any additional studies required by a Regulatory Authority or hospital ethics committee as a prerequisite to filing an IND.

1.36 **"Integrated Product Plan"** or **"IPP"** means a plan for the development, commercialization and marketing of a Collaboration Compound hereunder. The IPP will include Product charter, strategic intent, a market analysis (event maps - demographics, market dynamics), label need and wants (based on the applicable Development Plan), Product life overview, geographic overview, and financial overview. In addition, a global marketing plan will be developed and incorporated into the IPP which includes analysis of market (disease overview, Product profile, archetype, patient segmentation), strategic ends (strategic intent, product positioning, brand character, core messages, critical success factors, marketing objectives) strategic means (global Product, place, price, promotion, launch, market research programs), operational plan (implementation plan, marketing activities) and budget for the execution of the plan. Each IPP will also include appropriate milestones and the dates upon which such milestones must be met by ATL, as agreed upon by the parties hereto.

1.37 **"Invention"** has the meaning set forth in Section 8.1 herein.

1.38 **[***]** means all Patents owned by ISIS as of the Effective Date or during the Collaboration Term that claim any of [***].

1.39 **"ISIS Core Technology Patent Rights"** means the Patents owned by ISIS as of the Effective Date or during the Collaboration Term that claim ISIS Standard Chemistry, the cellular mechanisms of action by which phosphorothioate antisense oligonucleotides incorporating the ISIS Standard Chemistry exert their effect, or to methods of treatment using such oligonucleotides. ISIS Core Technology Patent Rights also include

the [***]. The ISIS Core Technology Patent Rights as of the Amendment Date are the Patents listed in Exhibit 1.39. Upon ATL's written request no more than once per year, ISIS will update Exhibit 1.39 and provide such updated exhibit to ATL.

1.40 **"ISIS Formulation Patent Rights"** means the Patents owned by ISIS as of the Effective Date or during the Collaboration Term that claim topical formulations incorporating antisense oligonucleotides made using ISIS Standard Chemistry, methods of making formulations containing such oligonucleotides for topical administration, or methods of treatment using such topical formulations. The ISIS Formulation Patent Rights as of the Amendment Date are the Patents listed in Exhibit 1.40.

1.41 **"ISIS FTE Rate"** means the compensatory rate to be paid per FTE at ISIS for all activities under this Agreement. As used herein, **"FTE"** means the equivalent of the scientific or technical work of at least a total of [***] on or directly related to the Collaborative Research Program or a Development Program hereunder, carried out by a qualified employee or consultant. Scientific or technical work can include, but is not limited to, [***] The ISIS FTE Rate is [***] for any of the following activities: [***].

1.42 **"ISIS Invention"** has the meaning set forth in Section 8.1(b).

1.43 **"ISIS Net Royalty"** means [***].

1.44 **"ISIS Patent"** has the meaning set forth in Section 8.1(b).

1.45 "**ISIS Patent Rights"** means all rights in Patents owned by ISIS that are within the ISIS Core Technology Patent Rights, the Manufacturing Patent Rights, the ISIS Formulation Patent Rights, or the Research Target Patent Rights.

1.46 **"ISIS Standard Chemistry"** means the technology, whether or not subject to a Patent, that is owned, acquired or controlled by ISIS as of the Effective Date or during the Collaboration Term that claims or covers linkages and sugar units in an antisense oligonucleotide, wherein such linkages include phosphorothioate linkages and such sugar units include a combination of deoxy sugar units and 2'-O-[methoxyethyl] (MOE) modified sugar units with natural and methyl substituted heterocycle bases ("MOE Gapmer Technology"). ISIS Standard Chemistry also includes the technology owned, acquired or controlled by ISIS as of the Effective Date that claims or covers the cellular mechanisms of action by which MOE Gapmer Technology antisense oligonucleotides exert their effect. ISIS Standard Chemistry does not include any target gene-specific technology.

1.47 **"Japanese Approval"** means the approval of a Product for marketing in Japan by the Japanese Ministry of Health and Welfare (or any future equivalent process), together with any other approval necessary to make and sell Product commercially in Japan without the requirement for price having been approved. If a Product can be sold in Japan without Ministry of Health and Welfare approval, Japanese Approval will be deemed to have been obtained on the first sale of a Product in Japan.

1.48 **"License to Exploit"** has the meaning set forth in Section 4.2.

1.49 **"License to Research"** has the meaning set forth in Section 4.1.

1.50 **"License Term"** has the meaning set forth in Section 4.0.

1.51 **"Major Market"** means any one of the following countries: the United States, Australia, Japan, the United Kingdom, France, Germany, Italy or Spain, except that [***] and [***] will not be considered Major Markets for the purposes of the License to Exploit the ATL 1102, VLA4 Compounds, Other VLA4 Compound and VLA4 Products.

1.52 **"Manufacture"** or **"Manufacturing"** or **"Manufactured"** means all operations involved in the manufacturing, quality control testing (including in-process, release and stability testing, if applicable), releasing, and shipping a Product.

1.53 **"Manufacturing Patent Rights"** means the Patents owned by ISIS as of the Effective Date or during the Collaboration Term that claim the Manufacturing Technology. The Manufacturing Patent Rights as of the Amendment Date are the Patents listed in Exhibit 1.53.

1.54 **"Manufacturing Process"** means the process steps set forth in master batch records for ATL 1102 in the version existing as of the Effective Date, including reasonable minor variants and extensions of process steps thereof.

1.55 **"Manufacturing Technology"** means any and all scientific and technical data and information including without limitation formulas, methods, techniques, protocols, and processes owned or controlled by ISIS as of the Effective Date or during the Collaboration Term which are necessary or useful for performing the Manufacturing Process.

1.56 **"Marketing Approval"** means the act of a Regulatory Authority necessary for the marketing and sale of the Product in a country or regulatory jurisdiction, including, without limitation, the approval of the NDA by the FDA, Australian Approval, EC/EMEA Approval, and Japanese Approval.

1.57 **"NDA"** means New Drug Application or similar application or submission for approval to market and sell a new pharmaceutical product filed with or submitted to a Regulatory Authority in conformity with applicable Regulatory Authority regulations.

1.58 **"Net Sales"** means, with respect to a Product, the gross amount invoiced by ATL or ISIS, as appropriate, or by their Affiliates or sublicensees, to unrelated Third Parties for the Product, less:

(a) Trade, quantity and cash discounts allowed;

(b) Commissions, discounts, refunds, rebates, chargebacks, retroactive price adjustments, and any other allowances which effectively reduce the net selling price;

(c) Credits for actual Product returns;

(d) Any tax imposed on the production, sale, delivery or use of the Product, including, without limitation, sales, use, excise or value added taxes;

(e) Allowance for distribution expenses at levels customary in the industry; and

(f) Any other similar and customary deductions.

"Net Sales" excludes:

(i) The transfer of reasonable and customary quantities of free samples of Product(s) and the transfer of Product(s) as clinical trial materials, other than for subsequent resale;

(ii) Sales or transfers of Product(s) among ATL and its Affiliates, unless the receiving party is the consumer or user of the Product; and

(iii) Use by ATL or its Affiliates or sublicensees of Product for any use connected with the securing of regulatory approval or validating of a manufacturing process or the obtaining of other necessary Marketing Approvals for Product (unless such Product is subsequently sold).

1.59 **[***]** means an Antisense Inhibitor, or other antisense inhibitor that [***].

1.60 **[***]**.

1.61 **"Original Agreement"** has the meaning provided in the "Introduction and Overview" set forth on the first page of this Agreement.

1.62 "**Other VL4A Compound**" means an Antisense Inhibitor, or other antisense inhibitor that incorporates other Antisense Technology, discovered by ISIS that (i) acts predominantly by hybridizing to CD49d or CD29 mRNA or pre-mRNA or that is designed to act by hybridizing to CD49d or CD29 mRNA or pre-mRNA, in each case to inhibit production of VLA4, and that incorporates ISIS Standard Chemistry, (ii) does not exist as of the Amendment Date and (iii) is not a VLA4 Compound.

1.63 **"Patent"** or **"Patents"** means (a) patent applications (including provisional applications and applications for certificates of invention); (b) any patents issuing from such patent applications (including certificates of invention); (c) all patents and patent applications worldwide based on, corresponding to, or claiming the priority date(s) of any of the foregoing; (d) any reissues, substitutions, confirmations, registrations, validations, re-examinations, additions, continuations, continued prosecution applications, continuations-in-part, requests for continued examination, or divisions of or to any of the foregoing; and (e) term extension or other governmental action which provide exclusive rights to a Product beyond the original patent expiration date.

1.64 **"Product"** means a VLA4 Product, any other Collaboration Compound Product or a Research Target Compound Product.

1.65 **"Regulatory Authority"** means any applicable government regulatory authority involved in granting approvals for the marketing and/or pricing of a Product worldwide including, without limitation, the United States Food and Drug Administration ("FDA") and any successor government authority having substantially the same function, and foreign equivalents thereof.

1.66 **"Research Services"** means discovery and design of Antisense Inhibitors of one or more Research Targets, supply of such Antisense Inhibitors to ATL, and/or evaluation of such Antisense Inhibitors in various functional assays.

1.67 **"Research Target"** means a gene product – usually, a protein – that may be modulated by another molecule, such as an antisense drug. Modulation of a Research Target may be accomplished in a variety of ways including, without limitation, the modulation of the synthesis, function or degradation of a Research Target, or the expression of the corresponding gene.

1.68 **"Research Target Compound"** means a compound that modulates a Research Target or Abandoned Research Target that was discovered by ATL alone or as part of a bona fide drug discovery collaboration with a Third Party in which ATL played a significant role.

1.69 **"Research Target Compound Product"** means a product containing a Research Target Compound.

1.70 **"Research Target Patent Rights"** means the Patents owned by ISIS as of the Effective Date or during the Collaboration Term that claim antisense oligonucleotides that modulate a Research Target, methods of making such oligonucleotides, or methods of treatment using such oligonucleotides. The Research Target Patent Rights thus include the VLA4 Compound Patent Rights set out in Exhibit 1.16. The Research Target Patent Rights will be updated from time to time as new Patents are added.

1.71 **"Sublicensee"** means any Third Party (including a distributor) to which ATL or any of its Affiliates grants any right to make, use, market, or import and sell a Product.

A Third Party who is granted only the right to import and sell a Product (such as a wholesaler) will not be considered a Sublicensee. Without limiting the generality of the foregoing, during the term of the Teva Sublicense, Teva will be considered a Sublicensee.

1.72 **"Sublicensee Market"** has the meaning set forth in Section 2.5(b)(ii) herein.

1.73 **"Sublicensee Product Plan"** or **"SPP"** has the meaning set forth in Section 2.5(b)(ii)(A) herein.

1.74 **"Sublicense Income"** means all consideration paid to ATL from Sublicensees pursuant to a sublicense by ATL or an Affiliate of ATL including, without limitation, up-front license fees, milestones, and royalties. If non-monetary consideration is received from Sublicensees by ATL or its Affiliates, then a commercially reasonable monetary value will be assigned for purposes of calculating Sublicense Income.

1.75 **"Technology"** means inventions (whether or not patentable), know-how, trade secrets, research tools, materials, and technical information, including but not limited to information in the form of research data, databases, experimental procedures, designs, formulas, and process information.

1.76 **"Teva"** has the meaning provided in the "Introduction and Overview" set forth on the first page of this Agreement.

1.77 **[***]**.

1.78 **"Teva/ISIS Agreements"** means that certain VLA4 Partner Support Agreement between ISIS and Teva and that certain Drug Supply, Manufacture and Technology Transfer Agreement between ISIS and Teva, each dated as of the Amendment Date.

1.79 **"Teva Sublicense"** has the meaning specified in the "Introduction and Overview" set forth on the first page of this Agreement.

1.80 **"Third Party"** means any party other than ISIS or ATL and their respective Affiliates.

1.81 **"Third Party Intellectual Property"** means any intellectual property owned by a Third Party.

1.82 **"Third Party Patent Rights"** means the [***].

1.83 **[***]**.

1.84 "**VLA4**" means the biological target known as [***].

1.85 **"VLA4 Compounds"** means Antisense Inhibitors, whether or not including ATL1102, discovered by ISIS that (i) are covered by any claim within the VLA4 Compound Patent Rights (including any Antisense Inhibitor targeting CD49d or CD29) and incorporate ISIS Standard Chemistry and (ii) exist as of the Amendment Date.

1.86 **"VLA4 Compound Patent Rights"** means the Research Target Patent Rights owned by ISIS as of the Amendment Date that claim ATL 1102, methods of making ATL 1102 for therapeutic use, or methods of using ATL 1102 for therapeutic applications, as listed in Exhibit 1.16 hereto.

1.87 **"VLA4 Product"** means a product containing ATL1102, a VLA4 Compound or Other VLA4 Compound as an active ingredient.

EXHIBIT 1.7

ANTISENSE INHIBITOR

ATL 1102

[***]

EXHIBIT 1.16

VLA4 Compound Patent Rights

[***]

EXHIBIT 1.31

[***]

EXHIBIT 1.32

[***]

EXHIBIT 1.39

[***]

EXHIBIT 1.40

[***]

EXHIBIT 1.53

[***]

EXHIBIT 1.59

[***]

EXHIBIT 1.80

[***]

EXHIBIT 3.4
RESEARCH TARGETS

[***]

EXECUTION VERSION *(02-08-08)*

CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R §§ 200.80(b)4, AND 240.24b-2

VLA4 PARTNER SUPPORT AGREEMENT

BY AND BETWEEN

ISIS PHARMACEUTICALS, INC.

AND

TEVA PHARMACEUTICAL INDUSTRIES LTD.

FEBRUARY 8, 2008

This VLA4 PARTNER SUPPORT AGREEMENT (the "Agreement"), entered into as of February 8, 2008 (the "Effective Date"), is made by and between ISIS Pharmaceuticals, Inc., a Delaware corporation with a principal place of business at 1896 Rutherford Road, Carlsbad, CA 92008 ("ISIS") and TEVA Pharmaceutical Industries Ltd., a limited liability company organized under the laws of Israel with its principal place of business at Petah Tiqva 49131, Israel ("TEVA").

BACKGROUND

A. ISIS and ATL entered into that certain collaboration and license agreement, dated October 30, 2001, which agreement was amended and restated on February 8, 2008 (the "Amended and Restated ISIS/ATL Agreement").

B. ATL and TEVA have agreed to enter into a license agreement dated as of even date hereof (the "ATL/TEVA Agreement").

C. In order to, among other things, induce TEVA to enter into the ATL/TEVA Agreement and to undertake its obligations thereunder, ISIS agrees to provide TEVA, in ISIS' capacity as licensor under the Amended and Restated ISIS/ATL Agreement, with:

(i) certain limited assurances and agreements supporting the assurances and agreements made by ISIS to ATL under the Amended and Restated ISIS/ATL Agreement and the assurances and agreements made by ATL to TEVA under the ATL/TEVA Agreement, and

(ii) support services in connection with the development of Products, as more fully described herein.

NOW, THEREFORE, for and in consideration of the representations, warranties and covenants hereinafter set forth, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged; it is agreed by and between the parties as follows:

1. DEFINITIONS

1.1 All capitalized terms used but not defined herein will have the meaning ascribed to such terms in the Amended and Restated ISIS/ATL Agreement.

1.2 Other Defined Terms. The following defined terms have the meanings set forth in the respective Sections referred to below:

Defined Term	Section
VLA4 Compounds/Products	2.1
ISIS/TEVA Meeting	3.1

ISIS Indemnitees	7.1(a)
Claims	7.1(a)
TEVA Indemnitees	7.1(b)
Indemnified Party	7.2
Indemnity Claim	7.2
Liaisons	10.3
Executives	10.12(a)
ICC	10.12(b)

1.3 Interpretation. The Section, Paragraph and other headings contained in this Agreement are for reference purposes only and will not affect the meaning or interpretation of this Agreement. All references in this Agreement to a Section or Paragraph will refer to a Section or Paragraph in or to this Agreement, unless otherwise stated. All references to a "party" is to a party to this Agreement Any reference to any federal, national, state, local, or foreign statute or law will be deemed also to refer to all rules and regulations promulgated thereunder, unless the context requires otherwise. The word "including" and similar words mean "including without limitation." The words "herein," "hereof' and "hereunder" and other words of similar import refer to this Agreement as a whole and not to any particular Section, Paragraph or other subdivision. References in this Agreement to "provisions of this Agreement"

refer to the representations, warranties and covenants contained in this Agreement taken as a whole. All references to days, months, quarters or years/annual are references to Business Days, calendar months, calendar quarters, or calendar years, respectively. References to the singular include the plural.

2. ASSURANCES REGARDING AMENDED AND RESTATED ISIS/ATL AGREEMENT

2.1 No Conflict. For the purpose of assuring and confirming to TEVA the rights and licenses granted to ATL in the Amended and Restated ISIS/ATL Agreement, ISIS will not enter into any agreement, without TEVA's prior written consent, which would impair or conflict with or adversely impact the rights and licenses granted by ISIS to ATL under the Amended and Restated ISIS/ATL Agreement with respect to ATL 1102, VLA4 Compounds or Other VLA4 Compounds and VLA4 Products (collectively, the "VLA4 Compounds/Products").

2.2 Further Amendment of the Amended and Restated ISIS/ATL Agreement. Without the prior written consent of TEVA, ISIS will not amend, modify or waive any provision of the Amended and Restated ISIS/ATL Agreement (including but not limited to the assignment provision thereof) in any manner that would (a) diminish any rights of ATL under the Amended

and Restated ISIS/ATL Agreement that would result in any direct or indirect diminution of TEVA's rights under the ATL/TEVA Agreement, (b) diminish any rights expressly conferred upon TEVA under the Amended and Restated ISIS/ATL Agreement or under this Agreement, or (c) directly or indirectly impose any additional financial or other obligations upon TEVA beyond those specified in this Agreement and the ATL/TEVA Agreement.

2.3 Material Default under the Amended and Restated ISIS/ATL Agreement.

(a) In the event of a default by ATL under the Amended and Restated ISIS/ATL Agreement that relates to VLA4 Compounds/Products (including, without limitation, any fundamental breach of the Amended and Restated ISIS/ATL Agreement by ATL with respect to which ISIS provides written notice to ATL under Section 12.2 thereof), ISIS will promptly inform TEVA in writing, and the parties agree that TEVA will have the right to cure such default on ATL's behalf.

(b) ISIS acknowledges and agrees that: (i) ISIS does not have the right to terminate the Amended and Restated ISIS/ATL Agreement except in the event ATL is in fundamental breach of its obligations thereunder (*i.e.*, a breach which goes to the heart of the Amended and Restated ISIS/ATL Agreement) and neither ATL nor TEVA has cured such breach within the period specified in Section 12.2(a) of the Amended and Restated ISIS/ATL Agreement; and (ii) a material breach of the Amended and Restated ISIS/ATL Agreement by ATL that is not fundamental gives rise solely to a right of damages but not a right to terminate the Amended and Restated ISIS/ATL Agreement.

(c) If ATL commits a fundamental breach of the Amended and Restated ISIS/ATL Agreement relating to VLA4 Compounds/Products, and ISIS provides written notice of such fundamental breach to ATL under Section 12.2(a) of the Amended and Restated ISIS/ATL Agreement, ISIS will concurrently provide a copy of such notice to TEVA, and TEVA will have the right to cure such breach on ATL's behalf within the applicable time period specified in such Section 12.2(a). If ATL cures such breach, or TEVA cures such breach on ATL's behalf, within the applicable time period specified in Section 12.2(a), ISIS will not have the right to terminate the Amended and Restated ISIS/ATL Agreement on the basis of such fundamental breach.

(d) If ATL commits a fundamental breach of the Amended and Restated ISIS/ATL Agreement unrelated to VLA4 Compounds/Products, and ISIS provides written notice of such fundamental breach to ATL under Section 12.2(a) of the Amended and Restated ISIS/ATL Agreement, ISIS will concurrently provide a copy of such notice to TEVA. Notwithstanding any failure by ATL to cure said fundamental breach within the applicable time period specified in such Section 12.2(a), ISIS acknowledges and agrees that such uncured fundamental breach will not give ISIS the right to terminate the Amended and Restated ISIS/ATL Agreement in its entirety, and that in such event, the Amended and Restated ISIS/ATL Agreement will: (A) terminate as it

relates to Research Targets other than CD49d and Collaboration Compounds other than VLA4 Compounds/Products; and (B) remain in full force and effect in accordance with its terms (including, without limitation, such Section 12.2) as it relates to CD49d and VLA4 Compounds/Products.

2.4 Other Termination of the Amended and Restated ISIS/ATL Agreement. Except as expressly set forth in Section 2.3 above or in Section 2.5 below, ISIS will not terminate the Amended and Restated ISIS/ATL Agreement prior to its expiration. However, if in fact the Amended and Restated ISIS/ATL Agreement is terminated for any reason with respect to VLA4 Compounds/Products resulting in the termination of the ATL/TEVA Agreement, then ISIS and TEVA shall enter into a ISIS/TEVA License Agreement as provided in Section 2.5 below.

2.5 Effect of TEVA's Curing of a Fundamental Breach by ATL and the Effect of ATL's Bankruptcy. In the event that (i) under Section 2.3 of this Agreement TEVA cures more than one fundamental breach relating to VLA4 Compounds/Products by ATL of the Amended and Restated ISIS/ATL Agreement or in the event that ATL commits a fundamental breach relating to VLA4 Compounds/Products of the Amended and Restated ISIS/ATL Agreement that is not capable of being cured by TEVA (e.g., a breach that is not monetary and may be performed only by ATL), or (ii) TEVA exercises its right to terminate the ATL/TEVA Agreement under Section 21.2(c) thereof, then ISIS shall terminate the Amended and Restated ISIS/ATL Agreement as it relates to VLA4 Compounds/Products and TEVA shall terminate the ATL/TEVA Agreement. In such event, ISIS and TEVA shall on an urgent basis negotiate in good faith and enter into an agreement (an "ISIS/TEVA License Agreement") substantially on the same non-financial terms and conditions (but on the exact same financial terms and conditions) as set forth in the Amended and Restated ISIS/ATL Agreement as it relates to VLA4 Compounds/Products, in effect substituting TEVA for ATL under those provisions of the Amended and Restated ISIS/ATL Agreement relating to VLA4 Compounds/Products. For the avoidance of doubt, so as not to interrupt the Exploitation by TEVA of the Licensed Rights with respect to VLA4 Compounds/Products during any period of negotiation and drafting of an ISIS/TEVA License Agreement, ISIS and TEVA shall conduct themselves as if the ATL/TEVA Agreement is in full force and effect, except that references to "ATL" in the those portions of the Amended and Restated ISIS/ATL Agreement that relate to VLA4 Compounds/Products shall be deemed references to "TEVA" as if the Amended and Restated ISIS/ATL Agreement (as it relates to VLA4 Compounds/Products) were between ISIS

and TEVA. By its signature below, ATL (x) acknowledges and agrees that the goal of allowing TEVA to Exploit VLA4 Compounds/Products as contemplated in the ATL/TEVA Agreement and allowing ISIS to receive royalties and other payments under the Amended and Restated ISIS/ATL Agreement is of such fundamental importance to TEVA and ISIS that any such termination of the Amended and Restated ISIS/ATL Agreement and the ATL/TEVA Agreement is fair, (y) consents to the provisions of this Section 2.5 and (z) agrees that it shall have no Claims against (A) TEVA or its Affiliates, agents, employees, officers or directors arising from or in connection with any such termination by TEVA of the ATL/TEVA Agreement or its entering into an ISIS/TEVA License Agreement (except that TEVA and its Affiliates, agents, employees, officers and directors shall not have the benefit of this clause (z) in the event that TEVA wrongfully exercises its termination right in contravention of Section 21.2(c) of the ATL/TEVA Agreement), or against (B) ISIS or its Affiliates, agents, employees, officers or directors arising from or in connection

with any such termination by ISIS of the Amended and Restated ISIS/ATL Agreement or its entering into an ISIS/TEVA License Agreement (except that ISIS and its Affiliates, agents, employees, officers and directors shall not have the benefit of this clause (z) in the event that ISIS wrongfully exercises its termination right in contravention of the Amended and Restated ISIS/ATL Agreement).

2.6 Notice under the Amended and Restated ISIS/ATL Agreement. ISIS agrees that all notices to ATL under the Amended and Restated ISIS/ATL Agreement (other than notices regarding matters that are unrelated to the VLA4 Compounds/Products and in ISIS' good faith judgment would not reasonably be expected to have an adverse impact on the development or commercialization of VLA4 Compounds/Products) will be copied to TEVA at the address set forth in Section 10.6 hereof.

3. FURTHER ASSURANCES AND SUPPORT

3.1 [***] Education and Support. ISIS will provide, [***] to TEVA, assistance, education and support reasonably requested by TEVA for up to (a) [***] hours per [***] for the period ending [***] following the Effective Date and (b) [***] hours per [***] for each [***] thereafter until TEVA files an NDA (or foreign equivalent in a Major Market) for a Product; provided, however, that hours not used in a [***] do not carry over to the next [***] (i.e., no banking of hours not used in a [***]). ISIS will also host, at [***] TEVA, an educational meeting for TEVA personnel (the "ISIS/TEVA Meeting") for up to [***], at a mutually agreeable time, after the Effective Date. The ISIS/TEVA Meeting will be in addition to the [***] support to be provided by ISIS for the month in which the meeting occurs. In addition, ISIS will provide to TEVA copies of existing reports or other existing information relating to VLA4 Compounds/Products that are in ISIS' possession and control that TEVA may reasonably request, including any such reports related to class effect. Such reports will be provided at no cost to TEVA, except that TEVA will reimburse ISIS' out-of-pocket costs incurred in providing the same.

3.2 [***] Education and Support. In addition to the assistance, education and support referenced in Section 3.1, ISIS will provide additional assistance, education and support as reasonably requested by TEVA from time to time hereafter, at [***] cost and expense, in accordance with a plan mutually agreed upon by the parties in writing (which agreement will not be unreasonably withheld), for (a) the regulatory aspects of [***] with respect to VLA4 Compounds/Products, (b) [***] with respect to VLA4 Compounds/Products, including the [***], (c) [***] issues/activities with respect to VLA4 Compounds/Products, including responding to queries submitted by TEVA with respect to the [***] built by ISIS with respect to VLA4 Compounds/Products in order for TEVA to gain the benefit of the information contained therein, and (d) such other matters related to VLA4 Compounds/Products as the parties may mutually agree in writing.

3.3 VLA4 Restrictive Covenant. In order to allow TEVA to fully Exploit its rights under the ATL/TEVA Agreement and as a material inducement for TEVA to enter into the ATL/TEVA Agreement, ISIS covenants and agrees that, during the term of this Agreement, ISIS will [***] of this Agreement and the Amended and Restated ISIS/ATL Agreement [***] with respect to [***] with respect to any [***]; provided, however, that if a VLA4 Product has not

been [***] (or such later date as is mutually agreed by the parties), then the provisions of this Section 3.3 shall terminate as of such date.

3.4 Certain Future Inventions and Intellectual Property. Pursuant to Section 4.2(c)(i)(A) of the Amended and Restated ISIS/ATL Agreement, ISIS has granted to ATL rights to certain future inventions.

4. ADDITIONAL TECHNOLOGY

4.1 Other VLA4 Compounds or Next Generation VLA4 Compounds. ISIS will have no obligation to generate for TEVA any Other VLA4 Compounds or Next Generation VLA4 Compounds, unless and until:

(a) TEVA and ISIS mutually agree in writing upon a research plan, which agreement shall not be unreasonably withheld, specifically describing the activities to be undertaken by ISIS, including the amounts to be reimbursed by TEVA to ISIS for performing such activities; and

(b) With respect to Next Generation VLA4 Compounds, TEVA and ISIS mutually agree in writing upon license terms (including, without limitation, milestones and royalties payable to ISIS) with respect to products developed utilizing such Next Generation VLA4 Compounds.

4.2 Access to Additional Technology. If, after the Effective Date and during the Term of this Agreement, ISIS creates, develops, comes to own, or acquires a license with the right to grant sublicenses thereunder, any new or additional ISIS Core Technology Patent Rights or Manufacturing Patent Rights, or any new or additional Technology that both (i) is necessary or useful for the development, manufacture or commercialization of VLA4 Compounds/Products and (ii) is or has been [***] and TEVA desires access to any of the foregoing rights for the purpose of development, manufacture or commercialization of VLA4 Compounds/Products, ISIS agrees to negotiate in good faith with ATL and TEVA regarding such access, provided that any licenses or sublicenses from ISIS to ATL or TEVA under such Patents and/or Technology are conditioned on ATL's or TEVA's (as applicable) agreement (a) to [***]; and (b) to abide by all terms of the agreement under which a third party license is granted to ISIS. Notwithstanding the foregoing, ISIS agrees to

provide to TEVA, [***], (i) any [***] that are used in ISIS' [***], and/or (ii) such ISIS technology that (A) is required for TEVA to be able to [***] and (B) ISIS is [***] for such required technology.

4.3 Updates. No more than once per calendar year at ISIS' facility in Carlsbad, California (or such other location as is agreed upon by the parties), upon the written request of, but at no cost to, TEVA, ISIS will present an update to a reasonable number of TEVA staff scientists on [***] and any [***] for VLA4 Compounds/Products (provided that TEVA will be responsible for the expenses incurred by TEVA personnel in attending such update). In addition, upon TEVA's written request no more than once per year, and at no cost to TEVA, ISIS will update Exhibit 1.39 to the Amended and Restated ISIS/ATL Agreement and provide such updated exhibit to TEVA.

5. REPRESENTATIONS, COVENANTS AND WARRANTIES.

5.1 Mutual Warranties. Each of ISIS and TEVA hereby represents and warrants to the other as of the Effective Date as follows:

(a) It is duly organized and validly existing under the laws of the jurisdiction of its incorporation. It has the requisite legal and company power and authority to conduct its business as presently being conducted and as proposed to be conducted by it and is duly qualified to do business in those jurisdictions where its ownership of property or the conduct of its business requires, in each case the failure to have such power, authority or qualification would have a material adverse impact upon the respective rights and obligations of the parties under this Agreement.

(b) It has all requisite legal and company power and authority to enter into this Agreement and to perform its obligations contemplated hereunder. All company actions on its part, its boards of directors or managers, or similar governing body and its equity holders necessary for (A) the authorization, execution, delivery and performance by it of this Agreement, and (B) the consummation of the transactions contemplated hereby, have been duly taken.

(c) This Agreement is a legally valid and binding obligation of it, enforceable against it in accordance with its terms.

(d) None of the execution and delivery of this Agreement, the consummation of the transactions provided for herein or contemplated hereby, or the fulfillment by it of the terms hereof or thereof, will (with or without notice or passage of time or both) (A) conflict with or result in a breach of any provision of the certificate or articles of incorporation or formation, by-laws, statutes, operating agreement or other governing documents of it, (B) result in a default, constitute a default under, give rise to any right of termination, cancellation or acceleration, or require any consent or approval (other than approvals that have heretofore been obtained) of any governmental authority or under any of the terms, conditions or provisions of any material note, bond, mortgage, indenture, loan, arrangement, license, agreement, lease or other instrument or obligation to which it is a party or by which its assets may be bound, or (C) violate any rule or regulation of any stock exchange on which such party's securities are listed applicable to it.

5.2 Additional Representations and Warranties of ISIS. ISIS hereby further represents and warrants to TEVA, regardless of any investigation by TEVA, that as of the Effective Date:

(a) ISIS has assigned to ATL, free and clear of all liens, claims and encumbrances of every kind or nature, all rights, title and interests in and to the VLA4 Compound Patent Rights;

(b) to the best of ISIS' knowledge as of the Effective Date, the VLA4 Compound Patent Rights are valid and enforceable and are not subject to any pending or threatened re-examination, opposition, interference or litigation proceedings, and all assignments and maintenance fees have been timely filed and paid with respect to the VLA4 Compound Patent Rights;

(c) to the best of ISIS's knowledge as of the Effective Date, the practice of the ISIS Core Technology Patent Rights, and the Manufacturing Technology to manufacture VLA4 Compounds, as currently manufactured by ISIS as of the Effective Date, does not infringe on any Third Party patents;

(d) to the best of ISIS' knowledge as of the Effective Date, without reference to a specific development plan and without any investigation, the ISIS Core Technology Patent Rights, ISIS Formulation Patent Rights, Manufacturing Patent Rights and VLA4 Compound Patent Rights, considered together, constitute all of the Patents controlled by ISIS (as of immediately prior to the Effective Date) that are necessary for the development and commercialization of the ATL1102 Compound and VLA4 Compounds using the ISIS Standard Chemistry;

(e) ISIS has not granted, directly or indirectly, any licenses or other rights under the VLA4 Compound Patent Rights to any Person other than ATL and its Affiliates;

(f) the Amended and Restated ISIS/ATL Agreement is in full force and effect and has not been modified or amended; and

(g) to the best of ISIS' knowledge as of the Effective Date, neither ISIS nor ATL is in material default under, and neither party claims or has grounds upon which to claim the other party is in material default under, the Amended and Restated ISIS/ATL Agreement.

5.3 Notice of Patent Infringement. ISIS will promptly advise TEVA if it becomes aware of any suspected or actual infringement of the VLA4 Compound Patent Rights by any Person or of any suspected or actual infringement by the VLA4 Compound Patent Rights of any rights of any Person. In addition, ISIS will notify TEVA of any final determination of any legal action of ISIS or known to ISIS involving the ISIS Core Technology Patent Rights

and/or the Manufacturing Patent Rights that, in each case, claim inventions used in the manufacture of VLA4 Compounds/Products then under development or being commercialized by or on behalf of TEVA.

5.4 Additional Covenant of the Parties. Each of the parties will not insist upon, claim, plead, or take any benefit under any local laws of any jurisdiction, other than the internal laws of the United States and the State of New York, that may be available to it, in order to prevent, delay, hinder or otherwise frustrate the enforcement by the other of any of the provisions of this Agreement. In furtherance of the foregoing, each of the parties waives any rights or benefits that may be available under any local laws of any jurisdiction (other than the

internal laws of the United States and New York) that are contrary to any provision of this Agreement.

5.5 Disclaimer. THE PARTIES EXPRESSLY DISCLAIM ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT OF THIRD PARTY RIGHTS, UNLESS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT.

6. CONFIDENTIALITY AND NONDISCLOSURE

6.1 Nondisclosure Agreement. The Non-Disclosure Agreement entered into by and between the parties on July 23, 2007 is hereby incorporated herein as if set forth in full, and the terms thereof will be deemed to apply to all information as may be disclosed by each of the parties during the term of this Agreement.

6.2 Publications. TEVA will have the right to review any paper proposed for publication by or with the authorization of ISIS that discusses VLA4 Compounds/Products, including oral presentations and abstracts, regardless of whether such paper or presentation includes any Confidential Information. ISIS will deliver a complete copy to TEVA at least [***] days prior to submitting the paper to a publisher. TEVA will review any such paper and give its comments to ISIS within [***] days of the delivery of such paper to TEVA. ISIS will consider in good faith any TEVA request to delete references to any rights specified herein and comply with any TEVA request to delete references to any TEVA Confidential Information in any such paper and agrees to withhold publication of same for an additional [***] days in order to permit the parties to obtain patent protection, if TEVA deems it necessary, in accordance with the terms of this Agreement. To the extent that any approval of TEVA is not forthcoming within the time periods set forth herein, the ISIS Liaison with confer with the TEVA Liaison regarding TEVA's approval. Notwithstanding the foregoing, ISIS will not have the right to publish or present any clinical trial results from trials of VLA4 Compounds/Products without the prior written consent of TEVA.

6.3 Public Announcements. If the parties mutually agree, they will issue a joint press release regarding the execution of this Agreement. Except as otherwise specified in this Agreement or required by law, neither party will originate any news release or other public announcement, written or oral, whether in the public press, or stockholders' reports, or otherwise, relating to this Agreement, and neither party will use the name, trademark, trade name, logo or likeness of the other party or its employees in any publicity, news release or disclosure relating to this Agreement, or its subject matter, without the prior express written permission of the other party. The foregoing prohibition against news release or other public announcement will not apply where such publication, presentation or other public announcement is required by law or the rules of any relevant stock exchange, as instructed by the party's outside legal counsel; provided, however, that in any such case the disclosing party will provide notice thereof to the other party with sufficient opportunity to respond and, to the extent feasible, to prevent or limit any such disclosure or to request confidential treatment thereof, and the receiving party will give reasonable assistance to the disclosing party to preserve the information

as confidential. The Liaisons will be the contact persons for the exchange of the proposed public disclosures for party review.

7. INDEMNIFICATION

7.1 Indemnification.

(a) TEVA will indemnify, defend and hold ISIS and its agents, employees, officers and directors (the "ISIS Indemnitees") harmless from and against any and all liability, damage, loss, cost or expense (including reasonable attorneys' fees) arising out of third party claims or suits (collectively, "Claims") related to (i) breach by TEVA of its representations, warranties or covenants set forth in this Agreement; or (ii) the development, manufacture, use, handling, storage, sale or other disposition of any VLA4 Compounds/Products by TEVA or any of its affiliates, contractors or sublicensees; *provided*, *however*, that TEVA's obligations pursuant to this Section 6.1(a) will not apply to the extent such Claims result from (A) the gross negligence or willful misconduct of any of the ISIS Indemnitees or (B) a breach by ISIS of its representations and warranties set forth in this Agreement.

(b) ISIS will indemnify, defend and hold TEVA and its affiliates and each of their respective agents, employees, officers and directors (the "TEVA Indemnitees") harmless from and against any and all Claims related to breach by ISIS of its representations, warranties or covenants set forth in this Agreement; *provided however*, that ISIS' obligations pursuant to this Section 6.1(b) will not apply to the extent that such Claims result from (A) the gross negligence or willful misconduct of any of the TEVA Indemnitees; (B) a breach by TEVA of its representations and warranties set forth in this Agreement, or (C) ISIS' performance of development or other activities with respect to VLA4 Compounds/Products on behalf of TEVA in accordance with TEVA's written instructions and specifications.

7.2 Procedure. A party will give the other party notice of any Claim upon which such party (the "Indemnified Party") intends to base an indemnification claim (an "Indemnity Claim"). The indemnifying party has the right to control the defense, settlement or disposition of any Indemnity Claim using counsel of its choice and on terms that it deems are appropriate, except that Indemnified Party may, at its own expense, participate in that defense, settlement or disposition using counsel of its own choice. With respect to the defense, settlement or disposition of an Indemnified Claim, the Indemnified Party will provide the indemnifying party, upon its request, with reasonable assistance and cooperation with respect to the Indemnified Claim. Without limiting the generality of the foregoing, indemnifying party may not cease to defend, settle or otherwise dispose of any Indemnity Claim without the

Indemnified Party's prior written consent, which consent may be unreasonably withheld, if, as a result thereof, the Indemnified Party would become subject to injunctive or other equitable relief.

7.3 Limitation of Liability. Notwithstanding any other provision of this Agreement to the contrary, in no event will ISIS' total liability under this Agreement (including, but not

limited to, liability under Section 7.1) exceed [***]; *provided, however,* that the foregoing limitation shall not apply in the case of (a) any knowing misrepresentation by ISIS under this Agreement, or (b) any knowing and intentional breach of any covenant made by ISIS under this Agreement.

8. TERM AND TERMINATION.

8.1 Term. This Agreement will expire upon the expiration or termination of both the Amended and Restated ISIS/ATL Agreement and the ATL/TEVA Agreement.

8.2 Insolvency or Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by ISIS or TEVA are, and will otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of right to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The parties agree that the parties, as licensees of such rights under this Agreement, will retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code. The parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either party under the U.S. Bankruptcy Code, the party hereto which is not a party to such proceeding will be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, and same, if not already in their possession, will be promptly delivered to them (i) upon any such commencement of a bankruptcy proceeding upon their written request therefor, unless the party subject to such proceeding elects to continue to perform all of its obligations under this Agreement, or (ii) if not delivered under (i) above, following the rejection of this Agreement by or on behalf of the party subject to such proceeding upon written request therefor by the non-subject party.

8.3 Survival. Expiration or termination of this Agreement will not relieve the parties of any obligation accruing prior to such expiration or termination. Sections 5.4 and 5.5, this Section 8.3 and Article 10 will survive expiration or termination of this Agreement. Any expiration or early termination of this Agreement will be without prejudice to the rights of either party against the other accrued or accruing under this Agreement prior to termination, including the obligations to make any payments that were due or had accrued immediately prior the effective date of such termination.

9. CHANGE OF CONTROL

9.1 Change of Control of Isis. ISIS acknowledges and agrees that in the event of a Change of Control of ISIS in which the Third Party acquiring control of ISIS or its assets relating to VLA4 Compounds/Products is [***], then: (a) ISIS (or the successor entity) will not be allowed to [***]; and (b) ATL will be prohibited from providing ISIS (or the successor entity) with [***], other than (A) reports and information required to be made available under Sections 5.6 and 5.8 of the Amended and Restated ISIS/ATL Agreement and (B) summary annual reports regarding TEVA's development and commercialization activities with respect to VLA4 Compounds/Products in sufficient detail to allow ISIS to ascertain ATL's compliance with its diligence obligations under the Amended and Restated ISIS/ATL Agreement.

9.2 Change of Control of ATL. In the event of a Change of Control of ATL in which the Third Party acquiring control of ATL or its assets relating to VLA4 Compounds/Products is [***], then TEVA agrees that it will continue to provide to ISIS all reports relating to the development or commercialization of VLA4 Compounds/Products that would have been delivered to ATL but for such Change of Control of ATL. ISIS agrees that it will hold all such reports and the information contained therein confidential to the same extent that ISIS would be required to hold such reports and information confidential pursuant to the Amended and Restated ISIS/ATL Agreement if received from ATL.

10. MISCELLANEOUS.

10.1 Payment Related to [***]. Within five (5) Business Days after ISIS' receipt of notice from ATL that ATL has [***], on or before [***].

10.2 Force Majeure. Neither party will be responsible or liable in any way for failure or delay in carrying out the terms of this Agreement resulting from any cause or circumstance beyond its reasonable control, including fire, flood, other natural disasters, war, interruption of transit, accident, explosion, civil commotion, and acts of any governmental authority; *provided*, that the party so affected will give prompt notice thereof to the other. No such failure or delay will terminate this Agreement, and each party will complete its obligations hereunder as promptly as reasonably practicable following cessation of the cause or circumstances of such failure or delay.

10.3 Liaisons. For purposes of coordinating activities between the parties under the Agreement, including, without limitation, sharing of press releases and publications for review, each party will appoint an individual to act as its liaison (each a "Liaison" and collectively, the "Liaisons"). A party may change its Liaison at any time by providing written notice to the other party along with contact information for the its new Liaison.

10.4 Agency. Neither party is, nor will be deemed to be, an employee, agent or legal representative of the other party for any purpose. Neither party will be entitled to enter into any contracts in the name of, or on behalf of the other party, nor will a party be entitled to pledge the credit of the other party in any way or hold itself out as having authority to do so.

10.5 Choice of Law. This Agreement will be governed and interpreted, and all rights and obligations of the parties will be determined, in accordance with the laws of the State of New York (USA), without regard to its conflict of laws rules.

10.6 Notices. All notices, requests, demands, waivers, consents, approvals or other communications to any party hereunder will be in writing and will be deemed to have been duly given if delivered personally to such party or sent to such party by facsimile transmission or by registered or certified

mail, postage prepaid, to the addresses listed below, or to such other address as the addressee may have specified in notice duly given to the sender as provided herein.

If to TEVA:
TEVA Pharmaceutical Industries Ltd.
5 Basel Street, P.O. Box 3190
Petah Tiqva 49131
Israel
Attn: Vice President, Global Innovative Pipeline Management
Fax: 972-3-926-7742

with a copy to:
TEVA's General Counsel, Uzi Karniel,
at the address of TEVA (Fax: 972-3-926-7429); and
Richard S. Egosi, Esq.
Senior Vice President and General Counsel

TEVA North America
1090 Horsham Road
North Wales, PA 19454-1090
Fax: (215) 591-8813

If to ISIS:
Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008
USA
Attention: Chief Operating Officer
Fax No.: +1 (760) 931-9639

With a copy to:
Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008
USA
Attention: General Counsel
Fax No.: +1 (760) 268-4922

Such notice, request, demand, waiver, consent, approval or other communications will be deemed to have been given as of the date so delivered, if sent by facsimile transmission, or five (5) days after so mailed.

10.7 Severability. Should one or more provisions of this Agreement be held unenforceable or in conflict with applicable law or regulation, the parties will substitute, by mutual consent, valid provisions for such invalid provisions which valid provisions in their economic effect are sufficiently similar to the invalid provisions that it can be reasonably assumed that the parties would have entered into this Agreement with such valid provisions. In case such valid provisions cannot be agreed upon, the invalidity of one or several provisions of this Agreement will not affect the validity of this Agreement as a whole, unless the invalid provisions are of such essential importance to this Agreement that it is to be reasonably assumed that the parties would not have entered into this Agreement without the invalid provisions.

10.8 Entire Agreement. This Agreement, along with any agreements referenced herein and that certain Drug Supply, Manufacture and Technology Transfer Agreement between the parties dated as of the Effective Date, each as amended from time to time, states the entire agreement reached between the parties with respect to the transactions contemplated hereby and may not be amended or modified except by written instrument duly executed by the parties. This Agreement replaces and supersedes any and all previous agreements and understandings between the parties regarding the subject matter hereof, whether written or oral (including, without limitation, that certain Letter of Agreement, dated August 8, 2007, by and among ISIS, TEVA and ATL).

10.9 No Waiver. The failure of either party to enforce at any time, or for any period of time, any provision of this Agreement will not be construed as a waiver of such provision or of the right of such party thereafter to enforce each and every provision.

10.10 Assignment; Binding Effect. This Agreement is personal to each party and neither party may assign, dispose of, transfer or delegate any of its rights, duties or obligations under this Agreement or any interest in this Agreement without the other party's prior written consent, which consent may not be unreasonably withheld, *except that* subject to the provisions of this Section 10.10, (a) either party may assign or delegate any or all of its rights and obligations under this Agreement to its affiliates without the other party's prior written consent; *provided,* that the assigning party remains primarily liable for the performance and nonperformance of its affiliate's duties and obligations under this Agreement and *provided, further,* that the non-assigning party does not incur or suffer any adverse tax or other financial consequences as a result thereof, and (b) either party may assign this Agreement without the other party's prior written consent to its successor in interest in connection with a merger, acquisition or sale of all or substantially all of such party's assets; and (c) TEVA may assign this Agreement without the prior written consent of ISIS to a successor in interest in connection with the sale of substantially all of the assets used primarily in its multiple sclerosis business or any other business of an indication being exploited hereunder; provided, that in all such cases such successor in interest agrees in writing to be bound by all of such party's obligations as assignee. This Agreement is binding upon, enforceable against, and inures to the benefit of the parties and their respective successors and permitted assigns. Any attempt by either party to assign or delegate any of the duties, responsibilities or other obligations of this Agreement that is not in compliance with this Paragraph 8.8 will be deemed to be null and void *ab initio.*

10.11 Counterparts. This Agreement may be executed in any number of counterparts each of which will be deemed to be an original and all of which taken together will constitute one and the same instrument.

10.12 Dispute Resolution.

(a) It is the objective of the parties to seek to resolve any issues or disputes arising under this Agreement in an expedient and amicable manner, if at all possible, and to that end the parties agree to abide by the following procedures set forth in this Section 10.12 to resolve any such issues or disputes. The parties initially will attempt to settle any such issue or dispute through good faith negotiations in the spirit of mutual cooperation between business executives with authority to resolve the dispute. Prior to taking action as provided in Section 10.12(b) of this Agreement, the parties will first submit such dispute to the Executive Vice President and Chief Financial Officer of ISIS and the Group Vice President of Global Innovative Resources of TEVA (collectively, the "Executives") for resolution. The Executives will attempt to resolve the dispute through good faith negotiations over a reasonable period of up to 60 calendar days, unless

the Executives mutually agree in writing to extend such period of negotiation. Such 60-calendar day period will be deemed to commence on the date the dispute was submitted to the Executives. The Executives will, if mutually agreed by the Executives, submit the dispute to

voluntary mediation at such place and following such procedures as the parties will reasonably agree. All negotiations pursuant to this Section 10.12(a) will be confidential, and will be treated as compromise and settlement negotiations for purposes of applicable rules of evidence.

(b) Any dispute that is not resolved by the parties by negotiation and/or mediation pursuant to Section 10.12(a) above will, upon the submission of a written request of either party to the other party, be submitted to binding arbitration before a single arbitrator in accordance with the then prevailing rules of the International Chamber of Commerce ("ICC").

(c) If the dispute involves technical issues, the arbitrator will be qualified in the field of pharmaceuticals research and development. If the parties cannot agree on an arbitrator within thirty (30) days of filing with the ICC, then the ICC will appoint one in accordance with its then prevailing rules.

(d) The arbitration will be held in New York, New York, USA. The decision and award of the arbitrator will be final and binding and the award so rendered may be entered in any court having jurisdiction in relation to the award, as a judgment of the court.

(e) Each party will pay one half of the fee charged by the arbitrator, and half of any charge payable in respect of the venue where the arbitration is conducted; provided, however, that in rendering its decision the arbitrator has the discretion to reallocate the aforementioned payments. The parties will otherwise each bear their own costs of arbitration.

(f) The decision of the arbitrator may be reduced to a judgment by any court of competent jurisdiction.

(g) Notwithstanding the above, to the full extent allowed by law, either party may bring an action in any court of competent jurisdiction for injunctive relief (or any other provisional remedy) to protect the parties' rights or enforce the parties' obligations under this Agreement pending final resolution of any claims related thereto in an arbitration proceeding as provided above. In addition, either party may bring an action in any court of competent jurisdiction to resolve disputes pertaining to the validity, construction, scope, enforceability, infringement or other violations of patents or other proprietary or intellectual property rights.

10.13 No Consequential Damages. IN NO EVENT SHALL EITHER ISIS OR TEVA OR THEIR AFFILIATES BE LIABLE FOR SPECIAL, INDIRECT, INCIDENTAL, PUNITIVE OR CONSEQUENTIAL DAMAGES, WHETHER BASED ON CONTRACT, TORT OR ANY OTHER LEGAL THEORY; *PROVIDED*, THAT THIS LIMITATION SHALL NOT LIMIT THE INDEMNIFICATION OBLIGATION OF SUCH PARTY UNDER THE PROVISIONS OF SECTION 6 FOR SUCH DAMAGES CLAIMED BY A THIRD PARTY.

IN WITNESS WHEREOF, the parties have caused this Agreement to be duly executed and delivered in duplicate originals as of the date first above written.

TEVA PHARMACEUTICAL INDUSTRIES, LTD.

By: /s/ Ruth Levy, Ph.D

Its: Vice President

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall

Its: COO & CFO

With respect to Section 2.5 and Section 10.1 only,

ANTISENSE THERAPEUTICS LTD.

By: /s/ Mark Diamond

Its: CEO

CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R §§ 200.80(b)4, AND 240.24b-2

EXECUTION VERSION

STRATEGIC ALLIANCE MASTER AGREEMENT

AMONG

IBIS BIOSCIENCES, INC.

ISIS PHARMACEUTICALS, INC.

AND

ABBOTT MOLECULAR INC.

January 30, 2008

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STRATEGIC ALLIANCE MASTER AGREEMENT

THIS STRATEGIC ALLIANCE MASTER AGREEMENT **(**this "Master Agreement") is made and entered into as of this 30th day of January, 2008, by and among Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"), Ibis Biosciences, Inc., a Delaware corporation ("Ibis"), Abbott Molecular Inc., a Delaware corporation ("AMI") and Affiliate of Abbott Laboratories, an Illinois corporation ("Abbott"). Ibis, Isis and AMI are sometimes referred to herein individually as a "Party," and collectively as the "Parties."

RECITALS

WHEREAS, Ibis, Isis and AMI wish to enter into a strategic alliance related to the Business;

WHEREAS, as part of this strategic alliance, AMI will make an investment in Ibis by purchasing the Shares pursuant to Section 2 of this Master Agreement;

WHEREAS, as a material inducement for AMI to enter into this Master Agreement and the other Transaction Documents, Ibis and Isis will grant to AMI certain additional rights pursuant to the Investor Rights Agreement, the form of which is attached hereto as Exhibit A (the "Investor Rights Agreement");

WHEREAS, as a material inducement to enter into this Master Agreement and the other Transaction Documents, Isis has granted to AMI an option to, in AMI's sole discretion, purchase all of the Capital Stock of Ibis (other than the Shares (and the Additional Shares if AMI elects to acquire the Additional Shares pursuant to the Call Option Agreement and the Stock Subscription Agreement)) pursuant to the Call Option Agreement, in the form attached hereto as Exhibit B (the "Call Option Agreement");

WHEREAS, as a material inducement to enter into this Master Agreement and the other Transaction Documents, Ibis has granted to AMI a subscription right to, in AMI's sole discretion, subscribe for and purchase the Additional Shares prior to the Cut-Off Date for an aggregate purchase price of $20,000,000 pursuant to the Stock Subscription Agreement, the form of which has been agreed to by the Parties and is attached as an exhibit to the Call Option Agreement (the "Stock Subscription Agreement"); and

WHEREAS, if AMI, in its sole discretion, exercises the Call Option, the Parties will consummate the purchase by AMI of all of the Capital Stock of Ibis (other than the Shares (and the Additional Shares if AMI exercises the Subscription Right and acquires the Additional Shares pursuant to the Call Option Agreement and the Stock Subscription Agreement)) pursuant to the Stock Purchase Agreement, the form of which has been agreed to by the Parties and is attached as an exhibit to the Call Option Agreement (the "Acquisition Agreement").

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, and covenants hereinafter set forth and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

AGREEMENT

SECTION 1. DEFINITIONS

Capitalized terms used and not otherwise defined herein have the meanings ascribed to such terms in this Section 1.

(a) "Abbott Transaction Team" means the individuals listed on Schedule 1(a).

(b) "Acquisition Closing" means the consummation of the purchase by AMI of all of the Capital Stock of Ibis (other than the Shares (and the Additional Shares if AMI elects to acquire the Additional Shares pursuant to the Call Option Agreement and the Stock Subscription Agreement)) pursuant to the Acquisition Agreement.

(c) "Additional Shares" means 114,250 shares of Common Stock that may be acquired by AMI from Ibis in AMI's sole discretion prior to 5:00 p.m. (Pacific Time) on the Cut-Off Date pursuant to the Call Option Agreement and the Stock Subscription Agreement, as may be held from time to time by AMI and its permitted assigns, which, together with the Shares, will represent approximately 18.6% of the issued and outstanding Common Stock.

(d) "Affiliate" of an entity means any other entity that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such first entity. For purposes of this definition only, "control" (and, with correlative meanings, the terms "controlled by" and "under common control with") means the possession, directly or indirectly, of the power to direct the management or policies of an entity, whether through the ownership of voting securities or by Contract relating to voting rights or corporate governance; *provided*, that (i) with respect to AMI and Abbott, the term "Affiliate" shall specifically exclude [***] and (ii) with respect to Isis, the term "Affiliate" shall specifically exclude [***]

(e) "Applicable Law" or "Law" means all applicable common law, laws, constitutional provisions, ordinances, statutes, rules, regulations, administrative rulings, executive orders and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, agency or other body, domestic or foreign, including but not limited to any applicable rules, regulations, guidelines, or other requirements of Governmental Authorities that may be in effect from time to time.

(f) "[***] Milestone" has the meaning ascribed to such term in the Call Option Agreement**.**

(g) "Business" means researching, developing, manufacturing, selling, marketing, distributing and using a system, process or reagents for the identification and/or quantitation of nucleic acids or the performing of services relating to the foregoing, as conducted by Ibis or by Isis, with respect to the Division, on and prior to the date hereof.

(h) "Business Day" means any day other than a Saturday, Sunday, or a day on which the banks in Chicago, Illinois are authorized or obligated by Law to close.

(i) "Call Option" has the meaning ascribed to such term in the Call Option Agreement.

(j) "Call Option Expiration Date" has the meaning ascribed to such term in the Call Option Agreement.

(k) "Call Period" has the meaning ascribed to such term in the Call Option Agreement.

(l) "Capital Stock" means all capital stock, equity or controlling interests and other securities in an issuer, including, without limitation, options, warrants, depositary receipts, stock appreciation or phantom stock rights or other agreements or undertakings, including stock or securities convertible or exchangeable for any shares of capital stock, equity or controlling interests or other securities in an issuer or containing any profit participation features or pursuant to which such issuer is or could be bound to issue or repurchase any capital stock, equity or controlling interests or other securities.

(m) "Change of Control" means, with respect to any Person, the occurrence of (i) any consolidation or merger of such Person with or into any other Person, or any other corporate reorganization or transaction (including the acquisition of Capital Stock of such Person (or any rights to acquire, or securities convertible into or exchangeable for, any such Capital Stock)), whether or not such Person is a party thereto, in which the stockholders or equity-holders of such Person or other Persons controlling such Person immediately prior to such consolidation, merger, reorganization or transaction, own Capital Stock either (A) representing directly, or indirectly through one or more entities, less than fifty percent (50%) of the economic interests in or voting power of such Person or other surviving entity immediately after such consolidation, merger, reorganization or transaction or (B) that does not directly, or indirectly through one or more entities, have the power to elect a majority of the entire board of directors or equivalent governing body of such Person or other surviving entity immediately after such consolidation, merger, reorganization or transaction or (ii) a sale, lease, license or other disposition of all or a material portion of the assets of such Person.

(n) "Claim" means any claim, lawsuit, demand, audit, investigation, charge, suit, hearing, notice of a violation, litigation, action, proceeding, order, judgment, grievance, or arbitration, whether civil, criminal, administrative or otherwise, whether at law or in equity, or any inquiry likely to

result in any of the foregoing.

(o) "Closing Date" means 9:00 a.m. Pacific Time on the date hereof.

(p) "Code" means the Internal Revenue Code of 1986, as amended from time to time.

(q) "Common Stock" means the Common Stock of Ibis, par value $0.001 per share.

(r) "Confidential Information" means all information and any tangible embodiments thereof provided by or on behalf of the Disclosing Party to the Receiving Party or to the Receiving Party's Representatives either in connection with the discussions and

negotiations pertaining to the Transaction Documents or in the course of performing the Transaction Documents, including without limitation: know-how; data; knowledge; practices; processes; research and development plans; engineering designs and drawings; research data; manufacturing processes and techniques; scientific, manufacturing, marketing and business plans; and financial and personnel matters relating to the Disclosing Party or to its present or future products, sales, suppliers, customers, employees, consultants, independent contractors, investors or business; regardless of whether any of the foregoing are marked "confidential" or "proprietary" or communicated to the other by the Disclosing Party in oral, written, graphic or electronic form. *Notwithstanding the foregoing*, information of a Party will not be deemed Confidential Information to the extent that the Receiving Party can show by competent proof that such information:

(i) is or becomes generally available to the public other than as a result of an unauthorized disclosure by the Receiving Party or its Representatives;

(ii) was available to the Receiving Party or its Representatives on a non-confidential basis prior to its disclosure by the Disclosing Party or its Representatives;

(iii) is or becomes available to the Receiving Party or its Representatives from a Person, other than the Disclosing Party or its Representatives, who is not bound by a confidentiality obligation to the Disclosing Party or its Representatives;

(iv) is independently developed by the Receiving Party or its Representatives without reference to or use of any Confidential Information of the Disclosing Party.

(s) "Contract" means any contract, lease, deed, mortgage, license, instrument, note, commitment, undertaking, understanding, indenture, joint venture, purchase order, service order and all other agreements and arrangements, whether oral or written.

(t) "Contribution Agreement" means the Contribution Agreement, dated July 31, 2007, by and between Ibis and Isis.

(u) "Corporate Services Agreement" means the Corporate Services Agreement, dated July 31, 2007, by and between Ibis and Isis.

(v) "Cut-Off Date" has the meaning ascribed to such term in the Call Option Agreement.

(w) "Division" means the Ibis Biosciences division of Isis.

(x) "Employee Pension Benefit Plan" has the meaning set forth in Section 3(2) of ERISA.

(y) "Employee Welfare Benefit Plan" has the meaning set forth in Section 3(1) of ERISA.

(z) "Encumbrance" means any mortgage, covenant, hypothecation, condition, Claim, easement, encroachment, right of way, restriction, option, lien (statutory or otherwise), pledge, charge, license, security interest or encumbrance of any nature whatsoever.

(aa) "Environmental Laws" means any federal, state, local or foreign statutes, ordinances, codes, treaties, or other Laws (including, without limitation, the Comprehensive Environmental Response, Compensation, and Liability Act, the Resource Conservation and Recovery Act, the Clean Air Act, the Clean Water Act, the Toxic Substances Control Act, the Oil Pollution Prevention Act, the Federal Insecticide, Fungicide, & Rodenticide Act, the Safe Drinking Water Act, the Hazardous Materials Transportation Act, the Solid Waste Disposal Act, the Emergency Planning and Community Right-to-Know Act, the Occupational Safety and Health Act), including any regulations, rules, plans, other criteria, policies or guidelines promulgated pursuant to such Laws, and all common law, orders, judgments, decrees, judicial or agency interpretations now or hereafter in effect relating to pollution, the generation, production, installation, use, storage, treatment, transportation, Release, threatened Release, investigation, monitoring, remediation, cleanup, abatement, removal, or disposal of Hazardous Materials, noise control, odor or the protection of public or workplace health or safety, natural resources, or the environment.

(bb) "ERISA" means the Employee Retirement Income Security Act of 1974, as amended.

(cc) "Escrow Agreement" means the Escrow Agreement to be attached as an exhibit to the Acquisition Agreement.

(dd) "Financing" means the sale of the Shares by Ibis to AMI pursuant to this Master Agreement, together with the other transactions contemplated hereby.

(ee) "Financing Closing" means the closing of the Financing under this Master Agreement.

(ff) "Fundamental AMI Representations" means those representations and warranties of AMI set forth in Section 3.2(a) (Power and Authority), Section 3.2(b) (Enforceability), Section 3.2(c) (Governmental Authority; Consents), and Section 3.2(d) (No Conflicts).

(gg) "Fundamental Isis Representations" means those representations and warranties of Ibis and Isis set forth in Section 3.1(a) (Power and Authority), Section 3.1(b) (Enforceability), Section 3.1(c) (Governmental Authority; Consents), Section 3.1(d) (No Conflicts), Section 3.1(e) (Due Organization; Qualification), Section 3.1(g) (Capitalization; Voting Rights), Section 3.1(j) (Title to Properties and Tangible Assets; Liens, etc.), Section 3.1(k) (Sufficiency of Assets), Section 3.1(m) (Compliance with Other Instruments) and Section 3.1(v) (Brokers' Fees).

(hh) "GAAP" means United States generally accepted accounting principles, applied on a consistent basis.

(ii) "Governmental Authority" means any governmental or quasi-governmental agency, department, bureau, office, center, institute, court, commission or other unit of the government of the United States of America or of any of its respective States or local units of government thereof, or of a foreign sovereign or of a provincial, regional or metropolitan government thereof, including, without limitation, any Regulatory Authority.

(jj) "Hazardous Materials" means any substance, chemical, solvent, compound, waste, residue, contaminant or other material which is regulated by or forms the basis of liability now or hereafter under any Environmental Law, including, without limitation: (i) any "solid waste," "dangerous goods," "hazardous waste," "hazardous substance," "hazardous material," "extremely hazardous waste," "pollutant," "contaminant," "hazardous constituent," "special waste," "universal waste," "toxic substance," or any other similar term or phrase as defined under any Environmental Law; (ii) any petroleum, or petroleum products, byproducts or breakdown products, including crude oil and any fraction thereof; (iii) natural synthetic gas usable for fuel; (iv) any asbestos, lead-based paint, polychlorinated biphenyl, mold, radon gas, radioactive material or byproduct, isomer of dioxin, or any material or thing containing or composed of such substance or substances; and (v) any virus, bacteria, protozoa, parasite, fungi, or other pathogen or any other substance, chemical, solvent, compound, waste, residue, contaminant or other material which is hazardous, toxic, poisonous, reactive, corrosive or otherwise may present a threat to human health, safety, natural resources, wildlife or the environment.

(kk) "Indebtedness" means (i) all indebtedness or other obligations of Ibis for borrowed money, whether current, short-term or long-term, secured or unsecured, and all accrued interest, premiums, penalties and other obligations relating thereto, (ii) all indebtedness of Ibis for the deferred purchase price of property or services which is not evidenced by accounts payable incurred in the ordinary course of business, (iii) all existing lease obligations of Ibis under leases which are capital leases in accordance with GAAP, (iv) any liability of Ibis under deferred compensation plans, phantom stock plans, severance or bonus plans, or any change in control or similar payment or increased cost which is triggered or made or will be made payable as a result of the transactions contemplated hereby, other than the Permitted Employee Compensation Plan, (v) any off balance sheet financing of Ibis, (vi) any payment obligations of Ibis in respect of banker's acceptances or letters of credit, (vii) any liability of Ibis with respect to interest rate swaps, collars, caps and similar hedging obligations, (viii) all obligations of Ibis arising under or with respect to any conditional sale or other title retention agreement with respect to property acquired by Ibis, (ix) past due or deferred rent of Ibis, (x) the amount of accounts payable owed by Ibis to any Person that have not been paid within forty-five (45) days of the date of invoice thereof (xi) any indebtedness referred to above of any Person which is either guaranteed by, or secured by a security interest upon any property owned by, Ibis and (xii) accrued and unpaid interest of, and prepayment premiums, penalties or similar contractual charges arising as a result of the discharge of any such foregoing obligation.

(ll) "Initial Offering" means Ibis' first firm commitment underwritten public offering of its Common Stock registered under the Securities Act.

(mm) "Intellectual Property" means all of the following in any jurisdiction throughout the world: (i) patents, patent applications and patent disclosures and statutory

invention registrations, including reissues, divisions, continuations, continuations in part, extensions and reexaminations thereof; (ii) trademarks, service marks, trade dress, trade names, corporate names, logos and slogans (and all translations, adaptations, derivations and combinations of the foregoing) and Internet domain names, any and all common law rights and registrations and applications for the registration thereof, and all extensions and renewals of any of the foregoing; (iii) copyrights and copyrightable works (including Software), registered copyrights and copyright applications, mask works, net lists and schematics; (iv) confidential and proprietary information including technology, know-how, trade secrets, unpatented inventions, ideas, algorithms and processes (including, without limitation, manufacturing and production processes and techniques, drawings, specifications, designs, plans, proposals, test data including pharmacological, biological, chemical, biochemical, toxicological and clinical test data, analytical and quality control data, stability data and customer and supplier lists and related information); (v) other intellectual property and proprietary information and (vi) all copies and tangible embodiments of the foregoing, such as instruction manuals, laboratory notebooks, prototypes, samples, specimens, studies and summaries.

(nn) "Investment Documents" means this Master Agreement, the Call Option Agreement, the Investor Rights Agreement and the Stock Subscription Agreement.

(oo) "Knowledge" and terms of similar meaning (including, without limitation, "is aware of") mean with respect to Ibis and Isis, the actual knowledge of any of the individuals set forth on Schedule 1(oo), after due investigation, including, without limitation, inquiry of Persons with subject matter knowledge, *provided* that (A) solely for purposes of Sections 3.1(l)(v), 3.1(l)(vi) and 3.1(l)(ix), "Knowledge" and terms of similar meaning (including, without limitation, "is aware of") mean the actual knowledge of any employee of Ibis or Isis, after due investigation, including, without limitation, inquiry of Persons with subject matter knowledge and (B) solely for purposes of Section 3.1(l), inquiry of Persons with subject matter knowledge shall include inquiry of the outside counsel involved in the development or prosecution of the Business IP or who conducted 'freedom to operate analyses' identified on Schedule 1(oo).

(pp) "Licenses" means all licenses, permits, certificates of authority, variances, authorizations, approvals, registrations, franchises, orders and similar consents issued by any Governmental Authority or other Person, *provided* that the term License shall not include any license or other right to use any Intellectual Property.

(qq) "Loss" means any loss, liability, demand, Claim, action, cause of action, cost, damage, material diminution in value, deficiency, Tax, penalty, fine or expense (including interest, penalties, reasonable attorneys' fees and expenses and all amounts paid in investigation, defense or settlement of any of the foregoing and the enforcement of any related rights), whether or not arising out of third party claims.

(rr) "Management Presentations" means the Management Presentations of Ibis delivered to AMI pursuant to Section 2(h).

(ss) "Material Adverse Effect" means any event, circumstance or state of facts which has, or would reasonably be expected to have, a material adverse effect on the

business, assets, condition (financial or otherwise), operations, operating results, employee relations, customer relations or supplier relations of Ibis or the Business.

(tt) "Multiemployer Plan" has the meaning set forth in Section 3(37) of ERISA.

(uu) "Offering Memorandum" means the Offering Memorandum of Ibis, dated November 2006 as made available to AMI.

(vv) "Permitted Employee Compensation Plan" means the compensation plan mutually agreed by the Parties regarding [***], the terms of which are described on Exhibit C attached hereto.

(ww) "Permitted Encumbrances" means (i) liens for current property Taxes not yet due and payable, (ii) Encumbrances arising in connection with and solely as a result of Permitted Indebtedness and (iii) except with respect to Intellectual Property, other imperfections of title, restrictions or Encumbrances, if any, which imperfections, restrictions or Encumbrances do not, individually or in the aggregate, impair the continued use and operation of the assets used in the operation of the Business and do not affect the merchantability of the title to such assets to which they relate.

(xx) "Permitted Indebtedness" means (i) accounts payable incurred in the ordinary course of business that are paid within forty-five (45) days of the date of invoice thereof, (ii) Indebtedness arising from existing and future lease obligations of Ibis under equipment leases that are capital leases in accordance with GAAP so long as the collateral for such capital leases is limited to the equipment acquired and the aggregate amount of such capital leases does not exceed $[***] and (iii) Indebtedness incurred pursuant to the Corporate Services Agreement or the Contribution Agreement.

(yy) "Person" means an individual, a partnership, a corporation, an association, a limited liability company, a joint stock company, a trust, a joint venture, an unincorporated organization, or a Governmental Authority (or any department, agency, or political subdivision thereof).

(zz) "Purchase Offer" means any proposal or offer from any Person (other than AMI and its Affiliates in connection with the transactions contemplated hereby) or any agreement or offer relating to any (i) reorganization, liquidation, dissolution, share exchange, business combination or recapitalization of Ibis, (ii) merger or consolidation involving Ibis, (iii) purchase or sale of any assets or Capital Stock of Ibis (other than the purchase and sale of inventory and capital equipment in the ordinary course of business), (iv) distribution of Ibis' existing or future products, (v) licensing of any Business IP from Ibis or (vi) any other transaction or business combination involving Ibis or its business or assets which would reasonably be expected to interfere with, impede or materially delay the transactions contemplated by the Transaction Documents or dilute the benefits thereof to AMI and its Affiliates. For the avoidance of doubt, the foregoing shall not apply to any transaction involving Isis and which only indirectly involves assets and/or Capital Stock of Ibis.

(aaa) "Real Property" means the Leased Real Property.

(bbb) "Regulatory Authority" means any Governmental Authority that has responsibility for granting any licenses or approvals or granting pricing and/or reimbursement approvals necessary for the marketing and sale of medical devices or diagnostic products, including without limitation, the FDA, the European Medicines Agency and the United States Department of Health and Human Services.

(ccc) "Release" means any spilling, leaking, pumping, pouring, emitting, emptying, discharging, injecting, escaping, leaching, dumping, depositing, disposing or other release into the environment (including the abandonment or discarding of barrels, drums, containers or other closed receptacles), including any dispersal, migration or other movement of any substance through or in air, soil, surface water, groundwater or property.

(ddd) "Representatives" means with respect to any Person, such Person's employees, directors, officers, Affiliates and authorized agents.

(eee) "SEC" or "Commission" means the United States Securities and Exchange Commission.

(fff) "Schedule" means any of the Disclosure Schedules delivered to AMI herewith and incorporated herein pursuant to Section 8.3(b) hereof.

(ggg) "Securities Act" means the Securities Act of 1933, as amended.

(hhh) "Shares" means 114,251 shares of Common Stock issued to AMI pursuant to this Master Agreement, as may be held from time to time by AMI and its permitted assigns, representing approximately 10.25% of the issued and outstanding Common Stock.

(iii) "Software" means any and all (i) computer programs, libraries, firmware and middleware, including any and all software implementations of algorithms, models and methodologies, whether in source code or object code, (ii) databases and compilations, including any and all data and collections of data, whether machine readable or otherwise, (iii) descriptions, flow-charts and other work product used to design, plan, organize and develop any of the foregoing and (iv) all programmer and user documentation, including user manuals and training materials, relating to any of the foregoing.

(jjj) "Subscription Right" has the meaning ascribed to such term in the Call Option Agreement.

(kkk) "T5000 Biosensor System" means the biosensor platform generally known as the T5000 Biosensor System, together with all equipment, hardware, Software, systems and other materials required for its use, or provided or recommended by Ibis, Isis or any of their respective Affiliates for its use, as well as all prior versions of the T5000 Biosensor System, including such systems known as "TIGER."

(lll) "Tax" means any federal, state, local, or foreign income, gross receipts, license, payroll, employment, excise, severance, stamp, occupation, premium, windfall profits, environmental, customs and other duties, Capital Stock, franchise, profits, withholding, social security, unemployment, disability, real property, personal property, sales, use, transfer,

registration, value added, alternative or add-on minimum, estimated, or other tax of any kind whatsoever, including any interest, penalty, or addition thereto, whether disputed or not, and including any obligation to indemnify or otherwise assume or succeed to the Tax liability of any other Person.

(mmm) "Tax Return" means any return, declaration, report, claim for refund, or information return or statement relating to Taxes, including any schedule or attachment thereto, and including any amendment thereof.

(nnn) "Transaction Documents" means this Master Agreement, the Investor Rights Agreement, the Stock Subscription Agreement, the Call Option Agreement, the Transition Services Agreement, the Escrow Agreement and the Acquisition Agreement.

(ooo) "Transfer" means, with respect to Capital Stock, any sale, pledge, hypothecation, assignment, Encumbrance or other transfer or disposition, whether directly, indirectly, voluntarily, involuntarily, by operation of Law, pursuant to judicial process or otherwise and, when the context so requires, the act of doing any of the foregoing.

(ppp) "Transition Services Agreement" means the Transition Services Agreement to be attached as an exhibit to the Acquisition Agreement.

Section references for definitions of defined terms defined in the body of this Master Agreement rather than in this Section 1.

Defined Term	Section
"Abbott"	Preamble
"Acquisition Agreement"	Recitals
"ADR"	8.1
"Business IP"	3.1(l)(i)
"AMI"	Preamble
"AMI Group"	7.2(a)
"Call Option Agreement"	Recitals
"Disclosing Party"	5.1
"Disclosure Schedules"	3.1
"ERISA Affiliate"	3.1(p)(ii)
"ERISA Plans"	3.1(p)(ii)
"FDA"	3.1(q)(i)
"Financial Statements"	3.1(t)
"Government Contracts"	3.1(l)(ii)
"Ibis"	Preamble
"Ibis Contracts"	3.1(x)(i)
"Indemnified Party"	7.2(c)
"Indemnifying Party"	7.2(c)

Defined Term	Section
"Insurance Policies"	3.1(y)
"Investor Rights Agreement"	Recitals
"IP Contracts"	3.1(l)(ii)
"Isis"	Preamble
"Leased Real Property"	3.1(w)(ii)
"Leasehold Improvements"	3.1(w)(ii)
"Leases"	3.1(w)(ii)
"Master Agreement"	Preamble
"Material Licenses"	3.1(q)(ii)
"Most Recent Balance Sheet"	3.1(t)
"Parties"	Preamble
"Party"	Preamble
"Plans"	3.1(p)(ii)
"Receiving Party"	5.1
"Remaining Shares"	3.1(g)(i)
"Seller Group"	7.2(b)
"Share Purchase Price"	2(d)
"Stock Subscription Agreement"	Recitals
"Third Party Claim"	7.2(c)

SECTION 2. FINANCING CLOSING; TRANSACTION DOCUMENTS

Subject to and upon the terms and conditions set forth in this Master Agreement, and in reliance upon the respective representations and warranties made herein by each of the Parties, at the Financing Closing:

(a) Ibis shall issue, sell, convey, assign, transfer and deliver to AMI a certificate representing the Shares sufficient to vest in AMI legal and beneficial ownership of the Shares, free and clear of all Encumbrances;

(b) Each Party shall execute and deliver to the other Parties the Call Option Agreement;

(c) Each Party shall execute and deliver to the other Parties the Investor Rights Agreement;

(d) AMI shall purchase, acquire and accept the Call Option, the Subscription Right and the Shares from Ibis and Isis for an aggregate purchase price of $20,000,000 (the "Share Purchase Price"), paid to Ibis via wire transfer of immediately available funds to an account designated by Ibis in writing;

(e) Ibis and Isis shall deliver to AMI a certificate, in a form reasonably acceptable to AMI, of an authorized officer of each certifying to and attaching thereto (i) Ibis' Certificate of Incorporation as in effect on the date hereof, (ii) Ibis' Bylaws as in effect on the date hereof and (iii) resolutions of the Board of Directors of Isis and Ibis authorizing the transactions contemplated by this Master Agreement and by the other Transaction Documents;

(f) Isis shall deliver to AMI the consent of Silicon Valley Bank to the Financing and the other transactions contemplated by the Investment Documents;

(g) Isis shall deliver to AMI one or more compact discs containing the contents of the electronic dataroom maintained by Isis at [***] as of January 23, 2008, together with a certificate of an authorized officer certifying that such compact discs contain true, accurate and complete copies of the materials in such dataroom as of such date; and

(h) Isis shall deliver to AMI one or more compact discs containing the Management Presentations of Ibis previously made available to AMI by Isis and Ibis.

SECTION 3. REPRESENTATIONS AND WARRANTIES.

3.1 Representations and Warranties of Ibis and Isis. As a material inducement to AMI to enter into this Master Agreement, except as set forth in the corresponding Section of the Disclosure Schedules delivered to AMI herewith on the date hereof (the "Disclosure Schedules"), Ibis and Isis each hereby jointly and severally represent and warrant as follows:

(a) Power and Authority. Each of Ibis and Isis (i) has the power, authority and the legal right to enter into this Master Agreement and the other Transaction Documents and to perform its obligations hereunder and thereunder, and (ii) has taken all necessary action required to authorize the execution and delivery of this Master Agreement and the other Transaction Documents and the performance of its obligations hereunder and thereunder.

(b) Enforceability. Each of this Master Agreement, the Call Option Agreement and the Investor Rights Agreement has been duly executed and delivered on behalf of Ibis and Isis and constitutes a legal, valid and binding obligation of each such Party and is enforceable against each such Party in accordance with its terms subject to the effects of bankruptcy, insolvency or other Laws of general application affecting the enforcement of creditor rights. If executed and delivered on the date hereof, the Stock Subscription Agreement and the Acquisition Agreement would constitute legal, valid and binding obligations of each of Ibis and Isis and would be enforceable against each in accordance with their terms subject to the effects of bankruptcy, insolvency or other Laws of general application affecting the enforcement of creditor rights.

(c) Governmental Authority; Consents. All necessary consents, approvals and authorizations of all Governmental Authorities and other parties required to be obtained by Ibis and Isis in connection with the execution and delivery of this Master Agreement and the other Investment Documents and the performance of their obligations hereunder and thereunder have been obtained.

(d) No Conflicts.

(i) The execution and delivery of this Master Agreement, the Call Option Agreement and the Investor Rights Agreement by each of Ibis and Isis and the performance of each such Party's obligations hereunder and thereunder, with or without the passage of time or giving of notice, (A) do not and will not conflict with or violate any requirement of Applicable Law or any provision of the certificate of incorporation, bylaws or any similar instrument of such Party, as applicable (B) do not and will not require any notice, conflict with, violate, or breach or constitute a default or require any consent or give rise to any termination or acceleration right or the creation of any Encumbrance on the Shares, the Additional Shares or the Remaining Shares or any of the properties or assets of Ibis under, any contractual obligation by which such Party is bound or subject to and (C) do not and will not cause the suspension, revocation, impairment, forfeiture or nonrenewal of any License applicable to Ibis, the Business or any of Ibis' operations, assets or properties.

(ii) If executed and delivered on the date hereof, the execution and delivery of the Stock Subscription Agreement and the Acquisition Agreement and the performance of Ibis' and Isis' obligations under each such agreement, with or without the passage of time or giving of notice, (A) would not conflict with or violate any requirement of Applicable Law or any provision of the certificate of incorporation, bylaws or any similar instrument of each such Party, as applicable, (B) would not require any notice, conflict with, violate, or breach or constitute a

default or require any consent or give rise to any termination or acceleration right or the creation of any Encumbrances on the Shares, the Additional Shares or the Remaining Shares under, any contractual obligation by which such Party is bound and (C) would not cause the suspension, revocation, impairment, forfeiture or nonrenewal of any License applicable to Ibis, the Business or any of Ibis' operations, assets or properties.

(e) Due Organization; Qualification. Each of Ibis and Isis is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, with full corporate power and authority to enter into this Master Agreement and the other Transaction Documents. Except as would not reasonably be expected to have a Material Adverse Effect, Ibis has obtained and currently maintains all qualifications to do business as a foreign corporation in all jurisdictions in which the character of the Business requires it to be so qualified. Ibis has all requisite power and authority and all authorizations and Licenses necessary to own, operate or conduct the Business.

(f) Subsidiaries. Ibis does not own or control any Capital Stock or other interest of any Person. Ibis is not a participant in any joint venture, partnership, limited liability company or similar arrangement. Since its inception Ibis has not merged with, acquired all or substantially all of the assets of (except pursuant to the Contribution Agreement) or acquired the Capital Stock of or any interest in any Person. Ibis does not hold the right to acquire any Capital Stock or interest in any other Person or have any obligation to make any investment in any Person and no such rights, Capital Stock or interests are necessary for the operation of the Business. Isis does not control or possess the power, directly or indirectly to control the management, actions or policies of [***].

(g) Capitalization; Voting Rights.

(i) The authorized Capital Stock of Ibis consists of 1,228,501 shares of Common Stock, par value $0.001 per share, 1,000,000 shares of which are issued and outstanding and held by Isis (the "Remaining Shares").

(ii) The issued and outstanding Capital Stock of Ibis as of the Financing Closing will consist exclusively of the Shares and the Remaining Shares. Except as set forth in the Investor Rights Agreement, Ibis does not have any obligations to issue or redeem any shares of Capital Stock, other than with respect to the Shares and the Additional Shares and Ibis has not issued any Capital Stock other than the Remaining Shares. No Capital Stock issued by Ibis is listed on any stock exchange or unregulated market. Other than the Investment Documents, there are no agreements with Isis or Ibis or any other Person with respect to the voting or Transfer of the Capital Stock.

(iii) The Shares and the Remaining Shares are: (A) duly authorized, validly issued, fully paid and nonassessable; (B) issued in compliance with all applicable state and federal Laws concerning the issuance of Capital Stock; and (C) free and clear of all Encumbrances other than the Call Option and the rights and obligations set forth in the Investor Rights Agreement; *provided*, that the Shares may be subject to restrictions on Transfer set forth in the Investor Rights Agreement and under state and/or federal securities Laws as set forth herein or as otherwise required by such Laws at the time a Transfer is proposed.

(iv) If AMI exercised the Subscription Right and acquired the Additional Shares on the date hereof, the Additional Shares would be: (A) duly authorized, validly issued, fully paid and nonassessable; (B) issued in compliance with all applicable state and federal Laws concerning the issuance of Capital Stock; and (C) free and clear of all Encumbrances other than the rights and obligations set forth in the Investor Rights Agreement; *provided*, that the Additional Shares may be subject to restrictions on Transfer set forth in the Investor Rights Agreement and under state and/or federal securities Laws as set forth in the Stock Subscription Agreement or as otherwise required by such Laws at the time a Transfer is proposed.

(v) Neither the sale of the Shares to AMI hereunder, nor the sale of the Additional Shares to AMI under the Stock Subscription Agreement, nor the sale of the Remaining Shares to AMI under the Acquisition Agreement is subject to any preemptive rights, rights of first refusal or similar rights.

(h) Agreements; Liabilities.

(i) There are no judgments, orders, writs or decrees to which Ibis or Isis is a party currently pending or, to Isis' or Ibis' Knowledge, threatened which would prevent Ibis or Isis from entering into the Transaction Documents or issuing or Transferring the Shares, the Additional Shares or the Remaining Shares pursuant to the terms of the Transaction Documents.

(ii) Ibis has not (A) accrued, declared or paid any dividends, or authorized or made any distribution upon or with respect to any class or series of its Capital Stock, (B) incurred or guaranteed any Indebtedness (other than Permitted Indebtedness), (C) made any loans or advances to any Person, other than advances for reasonable travel expenses to Ibis employees in the ordinary course of business, or (D) sold, exchanged, licensed or otherwise disposed of any of its tangible assets, other than the sale of its inventory in the ordinary course of business.

(iii) Ibis has no material obligations or liabilities (whether accrued, absolute, or to Isis' or Ibis' Knowledge contingent, unliquidated or otherwise, whether due or to become due and regardless of when or by whom asserted), including, without limitation, Taxes, except (A) obligations under the Ibis Contracts made available to AMI or under Contracts entered into in the ordinary course of business which, because of the dollar thresholds set forth in Sections 3.1(l) and 3.1(x), are not required pursuant to Sections 3.1(l) and 3.1(x) below to be described on Schedule 3.1(l) or Schedule 3.1(x) (but not liabilities for breaches of any such Contracts), (B) liabilities reflected on the Most Recent Balance Sheet, (C) liabilities and obligations which have arisen after the date of the Most Recent Balance Sheet in the ordinary course of business (none of which is material or is a liability for breach of contract, tort, infringement (directly, contributorily, by inducement or otherwise), Claim or warranty (other than warranty claims arising in the ordinary course of business in connection with the sale of Products or under Ibis Contracts made available to AMI, none of which warranty claims individually or in the aggregate would reasonably be expected to have a Material Adverse Effect) and (D) other liabilities and obligations to the extent expressly disclosed in Schedule 3.1(h)(iii).

(i) Obligations to Related Parties. There are no obligations of Ibis to Affiliates, officers, directors or employees of Ibis or Isis other than (A) for payment of salary to employees of Ibis for services rendered in the ordinary course of business, (B) reimbursement to employees of Ibis for reasonable expenses incurred in the ordinary course of business on behalf of Ibis, (C) standard employee benefits made generally available to all employees, pursuant to the Plans described on Schedule 3.1(p)(ii), (D) the Permitted Employee Compensation Plan or (E) Ibis' rights and obligations to Isis under the Contribution Agreement and Corporate Services Agreement. To Isis' and Ibis' Knowledge, all of the Contracts to which Ibis is a party or by which the Business or any of its assets is bound have been negotiated on an arms length basis.

(j) Title to Properties and Tangible Assets; Liens, Etc. Ibis has good and marketable title to its properties and tangible assets and good and valid title to its leasehold estates, in each case subject to no Encumbrance other than (i) Permitted Encumbrances and (ii) rights of the U.S. federal government in certain equipment purchased using government funds, as set forth on Schedule 3.1(j). The tangible assets of Ibis have been maintained in accordance with normal industry practice and are in good operating condition and repair (except for ordinary wear and tear).

(k) Sufficiency of Assets **(i)** Except for the services, funding and facilities provided under the Corporate Services Agreement, Ibis has all assets, properties and rights used in or necessary to operate or conduct the Business in all respects.

(ii) As of the date hereof, except for the services, funding and facilities provided under the Corporate Services Agreement and indirectly, via the Remaining Shares, Isis and its Affiliates do not have any right, title or interest in or to any asset, property, title or interest that is used in or necessary to operate or conduct the Business as conducted on and prior to the date hereof or as contemplated to be conducted by Ibis and Isis after the date hereof as reflected in the Offering Memorandum and Management Presentations. Pursuant to the Contribution Agreement, Isis has transferred to Ibis all assets, properties and rights Isis owned or which are or were used in or necessary to operate or conduct the Business except for the services, funding and facilities provided under the Corporate Services Agreement. No person employed by the Division prior to the date of the Contribution Agreement is currently employed by Isis and no former employee of Ibis or the Division is or has been employed by Isis.

(l) Intellectual Property.

(i) Schedule 3.1(l)(i) sets forth a complete and correct list of all of the following Intellectual Property used in or necessary to operate or conduct the Business (whether owned by Ibis or any other Person), and indicates with respect to each item, whether Ibis owns or licenses such Intellectual Property and the owner of any Intellectual Property covered by such license: (A) patented or registered Intellectual Property and pending patent applications or other applications for registrations of Intellectual Property (including jurisdiction, registration and application number, as applicable, and record owner), (B) registered and material unregistered trademarks, service marks, trade names, and Internet domain names, (C) Software (other than unmodified, commercially available, off-the-shelf Software purchased or licensed for less than an individual cost of $[***] and a total cost of $[***] in the aggregate for all such licenses), (D) material algorithms embodied in the Products and any other material trade secrets; and (E) all other material Intellectual Property used in or necessary to operate or conduct the Business (including, without limitation, all Intellectual Property set forth or required to be set forth in the following Schedules to the Contribution Agreement: Schedule 2.1 (Ibis Business Assets), Schedule 2.2 (Ibis Business Patents), Schedule 2.5 (Ibis Trademarks) and Schedule 2.6 (Ibis Business Software)) (all Intellectual Property described in the foregoing, (A) through (E), collectively, (without regard to whether such Intellectual Property is set forth on Schedule 3.1(l)(i)) "Business IP").

(ii) Schedule 3.1(l)(ii) sets forth a complete and correct list of all of the following Contracts (other than licenses for unmodified, commercially available, off-the-shelf Software purchased or licensed for less than an individual cost of $[***] and a total cost of $[***] in the aggregate for all such licenses) relating to the Business IP (collectively, the "IP Contracts"): (A) Contracts in which Ibis or Isis or any of their respective Affiliates is a licensee or sublicensee of Business IP; (B) Contracts in which Ibis or Isis or any of their respective Affiliates is a licensor or sublicensor of Business IP; (C) Contracts to which Ibis or Isis or any of their respective Affiliates is a party, or by which any of the Business IP is bound, that give any third party any right, title or interest in or to any such Business IP; (D) Contracts with any Governmental Authority wherein any portion of the Business IP was developed or used ("Government Contracts"); and (E) Contracts that restrict Ibis' rights in or use or disclosure of Business IP.

(iii) Ibis owns and possesses all right, title and interest in and to, free and clear of all Encumbrances (other than the rights of Governmental Authorities under Government Contracts identified in Schedule 3.1(l)(iii) to the Intellectual Property identified in such Schedule) or has a valid and enforceable license to use (pursuant to a written license agreement set forth and described in Schedule 3.1(l)(ii) or a written license for unmodified, commercially available, off-the-shelf Software purchased or licensed for less than an individual cost of $[***] and a total cost of $[***] in the aggregate) the Business IP.

(iv) Neither Isis nor any of its Affiliates (other than Ibis) has any right, title or interest in or to any of the Business IP.

(v) To Isis' or Ibis' Knowledge, neither Ibis, nor with respect to the Business, Isis, has infringed (directly, contributorily, by inducement or otherwise), misappropriated or otherwise conflicted with, and the operation of the Business (including the development, manufacture and commercialization of the T5000 Biosensor System and the assay kits specifically listed in the [***]) does not and will not infringe (directly, contributorily, by inducement or otherwise), misappropriate or otherwise conflict with, the patents, trademarks, copyrights or trade secrets of any Person, and neither Ibis nor Isis is aware of any facts that indicate a likelihood of any of the foregoing (including without limitation, oral or written demands or offers to license any Intellectual Property from any Person). With respect to whether the operation or conduct of the Business has or will infringe (directly, contributorily, by inducement or otherwise), misappropriate or otherwise conflict with patent, trademark, copyright or trade secrets of any Person (other than Ibis or Isis or their respective Affiliates), the Parties hereto are relying upon the representations and warranties contained in this Section 3.1(l)(v) and not the representations and warranties contained in Sections 3.1(k)(i), 3.1(l)(viii) or 3.1(l)(ix).

(vi) All of the Business IP is valid and, to Isis' or Ibis' Knowledge, enforceable. Isis and Ibis have taken all necessary actions to maintain and protect all of the Business IP, including, without limitation, entering into confidentiality agreements with each of its employees, consultants and independent contractors, and customers and vendors as necessary so as not to adversely affect the validity or enforceability thereof and have complied with disclosure requirements as provided by any Government Contract. Neither Ibis nor Isis has disclosed any source code for any Software included in the Business IP to any Person in a manner that would impair the trade secret or other Intellectual Property protection of such source code. There are no claims, oppositions or cancellation proceedings that either were made or brought within the past [***] years, or are presently pending or to Isis' or Ibis' Knowledge, threatened, against either Ibis or Isis contesting the validity, use, ownership, enforceability or registrability of any Business IP. Neither Ibis nor Isis is aware of any basis for any such claim, opposition or cancellation proceeding, and neither Ibis nor Isis has received any notices regarding any of the foregoing. No loss or expiration of any material Business IP is pending or reasonably foreseeable or to Isis' or Ibis' Knowledge, threatened, except for

patents expiring at the end of their statutory terms (and not as a result of any act or omission by either Ibis or Isis, including, without limitation, a failure to pay any required maintenance fees) or limitations to the scope of claims of any pending patent application made during the ordinary course of prosecuting such pending patent applications. Complete copies of all file histories for issued patents and pending patent applications of the Business IP owned or held by either Ibis or Isis have been provided to AMI.

(vii) To Isis' or Ibis' Knowledge, (A) no Person has infringed (directly, contributorily, by inducement or otherwise), or misappropriated any of the Business IP and (B) no Person is infringing (directly, contributorily, by inducement or otherwise) or misappropriating any of the Business IP.

(viii) Ibis has sufficient right, title and interest in and to the Business IP: (A) to conduct the Business, including the development, manufacture and commercialization of the T5000 Biosensor System and the assay kits specifically listed in the [***] on a worldwide basis, with no payment obligation to any Person, except pursuant to an IP Contract made available to AMI, and (B) to make, have made, import, use**,** offer for sale, or sell any product(3) currently marketed by the Business and the assay kits specifically listed in the [***] without infringing (directly, contributorily, by inducement or otherwise), misappropriating or conflicting with any Intellectual Property rights of any Person. As of the date hereof, the Business IP is owned by or available for use by Ibis on terms and conditions identical to those under which it was owned or used by Ibis and the Business prior to the date hereof.

(ix) To Isis' or Ibis' Knowledge, Ibis has sufficient right, title and interest in and to the Business IP: (A) to develop, manufacture and commercialize the [***] [***] [***] on a worldwide basis, with no payment obligation to any Person, except pursuant to an IP Contract made available to AMI, and (B) to make, have made, import, use, offer for sale, or sell the [***] [***] [***] without infringing (directly, contributorily, by inducement or otherwise), misappropriating or conflicting with any Intellectual Property rights of any Person.

(x) No funding, facilities or resources of a Governmental Authority, university, college, other educational institution or research center or funding from third parties was used in the development of any of the Business IP and no Governmental Authority, university, college, other educational institution or research center has any claim or right in or to any of the Business IP.

(xi) Each current or former employee of each Isis Party or any of their respective Affiliates, who was involved in, or who contributed to, the creation or development of any Business IP, executed the standard form of proprietary rights agreement set forth in Schedule 3.1(l)(xi) upon commencement of his or her employment and each such current or former employee and any consultant or independent contractor who was involved in, or who contributed to, the creation or development of any Business IP has validly assigned all right, title and interest in and to such Business IP to Ibis.

(xii) None of the Transaction Documents nor the transactions contemplated by any of the Transaction Documents would result in or reasonably be expected to result in: (A) Ibis, AMI or any of their respective Affiliates granting to any Person any right to or with respect to any Intellectual Property owned by, or licensed to, any of them as a result of any Encumbrance or Contract to which, Isis, Ibis or any of their Affiliates is a party or bound by, (B) other than standard non-solicitation agreements entered into in the ordinary course of business and made available to AMI, Ibis, AMI or any of their respective Affiliates being bound by, or subject to, any non-compete or other material restriction on the operation or scope of their respective businesses as a result of any Encumbrance or Contract to which Isis, Ibis or any of their Affiliates is a party or bound by, (C) other than as contemplated by the Acquisition Agreement, Ibis, AMI or any of their respective Affiliates being obligated to pay any royalties or other material amounts, to increase or accelerate any royalty or payment obligation, or to offer any discounts, to any Person as a result of any Encumbrance or Contract to which Isis, Ibis or any of their Affiliates is a party or bound by, or (D) any adverse effect on Ibis' right, title or interest in and to any of the Business IP.

(xiii) All components of the current version of the T5000 Biosensor System perform in all material respects in accordance with their currently advertised, displayed, distributed or published specifications. All services that have been performed in the conduct of the Business were performed in material conformity with the terms and requirements of the related Contracts and all Applicable Laws. All Software included in the Business IP is free of any disabling codes or instructions, timer, copy protection device, clock, counter or other limiting design or routing and any "back door," "time bomb," "Trojan horse," "worm," "drop dead device," "virus" or other similar disabling codes, Software routines or hardware components. No open source, public source or other Software that is licensed pursuant to a license that purports to require the distribution of, or access to, source code or purports to restrict one's ability to charge for distribution of Software (including, without limitation, any version of any Software licensed pursuant to any GNU general public license or limited general public license or other Software), was used in, incorporated into, integrated or bundled with any Software that has been used in the T5000 Biosensor System or any other product that has been distributed or is currently distributed. Ibis does not have any plans to include any such Software in any such system or Product.

(xiv) Without limiting any other representation or warranty herein, the computer and other information technology systems and networks owned or contracted for by Ibis have been maintained in accordance with normal industry practice, are in good operating condition and repair (except for ordinary wear and tear) and are sufficient for the operation of the Business. Each of Ibis and Isis has taken all

reasonably necessary action to safeguard the computer and other information technology systems and networks used in the operation of the Business and there has been no unauthorized intrusions or breaches of the security of the computer and other information technology systems and networks used in the Business that have materially compromised or are currently materially compromising the security, integrity or operations of such systems or networks.

(xv) The individuals identified as the outside counsel involved in the development or prosecution of the Business IP on Schedule 1(oo) represent the outside counsel who have provided Isis or Ibis strategic legal and Intellectual Property advice related to the Business IP and the Ibis Business during the three (3) years prior to the date hereof.

(m) Compliance with Other Instruments. Neither Ibis nor, with respect to the Business, Isis is in violation or default of any term of its charter documents, each as amended, or of any provision of any Contract to which it is party or by which the Business is bound or of any judgment, decree, order or writ.

(n) Litigation. There is no Claim pending or, to Isis' or Ibis' Knowledge, threatened against Ibis or, with respect to the Business, Isis (or against any Ibis or Isis employee (in their capacity as such)), at Law or in equity, or before or by any Governmental Authority, and to Isis' or Ibis' Knowledge, there is no reasonable basis for any of the foregoing. Neither Ibis nor, with respect to the Business, Isis is subject to any outstanding order, judgment, or decree issued by any Governmental Authority or any arbitrator. Neither Ibis nor any of its Affiliates has received any opinion or memorandum or advice from legal counsel to the effect that Ibis or the Business is or was exposed, from a legal standpoint, to any material liability.

(o) Tax Matters.

(i) Prior to the date hereof, Ibis has not been required to file any Tax Returns. All Taxes owed and due by Ibis have been paid. No claim has ever been made by an authority in any jurisdiction that Ibis is or may be subject to taxation by that jurisdiction. There are no Encumbrances on any of the assets used by Ibis that arose in connection with any failure (or alleged failure) to pay any Tax. Schedule 3.1(o)(i) contains a list of states, territories and jurisdictions (whether foreign or domestic) in which Ibis is required to file Tax Returns.

(ii) Ibis has withheld and paid all Taxes required to have been withheld and paid in connection with amounts paid or owing by Ibis to any employee, independent contractor, creditor, stockholder, or other third party, and all Forms W-2 and 1099 required with respect thereto have been properly completed.

(iii) There is no dispute or claim concerning any Tax liability of Ibis either (A) claimed or raised by any Governmental Authority or (B) as to which Isis or Ibis has Knowledge.

(iv) Neither Ibis nor, with respect to the Business, Isis, has waived any statute of limitations in respect of Taxes or agreed to any extension of time with respect to a Tax assessment or deficiency.

(v) To Isis' or Ibis' Knowledge based in good faith on advice of Deloitte & Touche LLP, (A) Ibis and Isis are and will be members of the same consolidated group, as such term is defined by Treasury Regulation § 1.1502-1(h), with Isis being the common parent of such consolidated group for all taxable years through and including the Acquisition Closing and (B) unless the provisions of the Code

pertaining to filing Tax Returns as a consolidated group are amended prior to the Acquisition Closing, Ibis and Isis will be eligible to file a consolidated Tax Return in lieu of separate Tax Returns with respect to income Tax imposed by Chapter 1 of the Code for all taxable years through and including the Acquisition Closing.

(vi) Ibis is not and will not at the Acquisition Closing be a party to any oral or written Tax sharing agreements or arrangements.

(p) Employees.

(i) Neither Ibis nor, with respect to the Business, Isis, is party to any collective bargaining agreement. There is no labor union organizing activity pending or, to Isis' or Ibis' Knowledge, threatened with respect to Ibis. Each of Ibis and, with respect to the Business, Isis has complied with all applicable Laws relating to the employment of labor and, within the last five (5) years, neither Ibis nor Isis, with respect to the Business, has experienced any strike, work stoppage, lockout, grievance, unfair labor practice claim or other labor relation problem, including, without limitation, any written dispute with or Claim by former employees regarding termination and/or severance pay. To the Knowledge of Isis or Ibis, no executive, key employee or group of employees of Ibis has any plans to terminate employment with Ibis. In the past three (3) years, Ibis and Isis have complied in all respects with the notification provisions (or paid severance in lieu thereof) of the WARN Act and applicable similar state or local laws. No executive, key employee or group of employees of Ibis or the Business has been terminated or resigned their employment since January 1, 2007.

(ii) Schedule 3.1(p)(ii) contains a true and complete list of each employment (other than at-will offer letters with no severance, compensation term guarantee or material benefit), bonus, fringe benefit, deferred compensation, incentive compensation, stock purchase, stock option, stock appreciation right or other stock-based incentive, severance, change-in-control, or other termination pay, hospitalization or other medical, disability, life or other insurance, supplemental unemployment benefits, profit-sharing, pension, or retirement plan, program or Contract and each other employee benefit plan, program or Contract sponsored, maintained or contributed to or required to be contributed to by Ibis, or by any trade or business, whether or not incorporated (an "ERISA Affiliate"), that together with Ibis or Isis would be deemed a "single employer" under Section 414(b), (c), (m) or (o) of the Code, for the benefit of any current or former employee or director of Ibis (the "Plans"). Schedule 3.1(p)(ii) identifies each Plan that is an "employee welfare benefit plan" or "employee pension benefit plan" as such terms are defined in Sections 3(1) and 3(2) of ERISA (such plans being hereinafter referred to collectively as the "ERISA Plans").

(iii) Neither Ibis nor Isis has any formal plan or binding commitment to create any additional Plan or modify or change any existing Plan that would affect any current or former employee or director of Ibis, except as required by Applicable Law or to conform such Plan to the requirements of any Applicable Law. Except for this Master Agreement, there are no Contracts, written or oral, or omissions that would prevent or impair any Plan (including any Plan covering retirees or other

former employees) from being amended or terminated by Ibis or Isis prior to or at the Acquisition Closing or, with respect to the Plans listed on Schedule 3.1(p)(xii) if any, by Ibis or AMI (or any successor thereto) on or at any time after the Acquisition Closing.

(iv) Neither Isis nor Ibis has incurred and has no reason to expect that either will incur any liability to the Pension Benefit Guaranty Corporation (other than premium payments) or otherwise under Title IV of ERISA (including any withdrawal liability) or under the Code or any Applicable Law with respect to any employee pension benefit plan that Isis or Ibis, or any other entity that together with Isis or Ibis is treated as a single employer under Section 414 of the Code, maintains or ever has maintained or to which it contributes, ever has contributed, or ever has been required to contribute.

(v) Neither Ibis nor Isis, nor any of the ERISA Plans, nor any trust created thereunder, nor to Isis' or Ibis' Knowledge, any trustee or administrator thereof has engaged in a transaction or has taken or failed to take any action in connection with which Ibis could be subject to any material liability for either a civil penalty assessed pursuant to Sections 409 or 502(i) of ERISA or a tax imposed pursuant to Sections 4975, 4976 or 4980B of the Code.

(vi) Each Plan is in all material respects in compliance, and has been administered in all material respects in accordance, with the applicable provisions of ERISA, the Code and all other Applicable Laws, including, but not limited to, medical continuation under section 4980B of the Code. Neither Isis nor Ibis has (A) engaged in any transaction prohibited by ERISA or the Code; (B) breached any fiduciary duty owed by it with respect to the Plans; or (C) failed to file and distribute timely and properly all reports and information required to be filed or distributed in accordance with ERISA or the Code.

(vii) Other than routine claims for benefits, there are no Claims, Internal Revenue Service or Department of Labor compliance programs or other proceedings pending or, to Isis' or Ibis' Knowledge, threatened against or otherwise involving any Plan.

(viii) Each Plan which is intended to be qualified under Section 401(a) of the Code (A) has been amended to reflect all requirements under the Code which are required to be adopted prior to the end of the applicable remedial amendment period and (B) has received from the Internal Revenue Service a favorable determination letter which considers the terms of the Plan as amended for such changes in Law.

(ix) None of the Plans obligates Isis or Ibis either (A) to pay any separation, severance, termination or similar benefit to Ibis Employees or (B) to make an excess parachute payment within the meaning of Code Section 280G.

(x) No Plan provides benefits, including without limitation death or medical benefits (whether or not insured), with respect to current or former employees of Ibis after retirement or other termination of service (other than

(A) coverage mandated by any Applicable Law, (B) death benefits or retirement benefits under any employee pension benefit plan or (C) benefits, the full direct cost of which are borne by the current or former employee (or beneficiary thereof)).

(xi) As of the date hereof, to Isis' or Ibis' Knowledge, other than as provided under the terms of the Plans, neither Ibis nor Isis has made any representation or commitment to, or entered into any formal or informal understanding with, any Ibis employee with respect to compensation, benefits, or terms of employment to be provided by AMI or Ibis or any of their respective Affiliates at or subsequent to the Acquisition Closing.

(xii) Except for the Permitted Employee Compensation Plan, Ibis neither sponsors nor maintains nor has any liability for (A) any of the Plans or (B) any other employee benefit plans or arrangements.

(xiii) All contributions, premiums or payments under or with respect to each Plan which are or were due on or before the date hereof have been paid.

(q) Compliance with Laws; Licenses.

(i) Ibis, the Business and, with respect to the Business, Isis are not in material violation of any Law. Ibis, the Business, and, with respect to the Business, Isis and Ibis' and Isis' Representatives have complied with, and are in material compliance with, all Applicable Laws, including, without limitation, the federal Food, Drug, and Cosmetic Act, as amended and regulations promulgated thereunder, and all U.S. Food and Drug Administration ("FDA") or its foreign equivalent regulations governing, among other things, the protection of human subjects and regulations governing clinical investigators. Except such as must be made after the Financing Closing (or, with respect to the Additional Shares, the Subsequent Closing), which will be filed in a timely manner, no governmental orders, permissions, consents, approvals or authorizations are required to be obtained and no registrations or declarations are required to be filed in connection with the execution and delivery of the Investment Documents, the issuance of the Shares or, if issued on the date hereof, the Additional Shares or, except as contemplated by the Acquisition Agreement, the Transfer of the Remaining Shares.

(ii) Ibis holds all Licenses necessary for the operation or conduct of the Business (including pursuant to Environmental Laws). Schedule 3.1(q)(ii) sets forth a list of all Licenses material to the Business (the "Material Licenses"). Ibis is and has been in compliance with all terms and conditions of such Material Licenses and all Material Licenses may be relied upon by Ibis for the lawful operation of

the Business as conducted on and prior to the date hereof and immediately following the Financing Closing. Each Material License is valid, binding and in full force and effect and Ibis and the Business have complied in all material respects with all requirements of and are not in default under any Material License and have not received written or, to Isis' or Ibis' Knowledge, oral notice that the Business or Ibis is in violation of any of the terms or conditions of such Material License. No loss or suspension of any License nor any

proceeding or investigation which is seeking such a loss or suspension is pending or, to Isis' or Ibis' Knowledge, threatened. Neither Ibis nor Isis is operating under any written or oral formal or informal agreement or understanding with any licensing authority, Regulatory Authority or any other Governmental Authority which restricts the conduct of the Business or requires Ibis or, with respect to the Business, Isis, to take or refrain from taking any actions.

(r) Environment, Health and Safety. Ibis and the Business have at all times materially complied with and are in material compliance with all Environmental Laws, including, without limitation, all Licenses and other authorizations that are required pursuant to Environmental Laws for the ownership and occupation of the assets used by Ibis and the operation of the Business. Neither Ibis nor Isis, with respect to the Business is aware of or has reason to be aware of or has received any notice, request for information, report, order, directive, communication or other information, written or oral, regarding any actual or alleged violation of Environmental Laws, or any Claims or other liabilities or potential liabilities (whether accrued, absolute, contingent, unliquidated or otherwise) arising under Environmental Laws, relating to the Business, the Real Property or Ibis, which has not been resolved without liability to Ibis. Neither Ibis nor its Affiliates nor any of its legal predecessors has, in violation of Environmental Laws, treated, stored, disposed of, arranged for or permitted the disposal of, transported, handled, or Released, or exposed any Person to, any Hazardous Materials, or owned or operated any property or facility (and no such property or facility including the Real Property is contaminated by any such Hazardous Materials) so as to give rise to any current or future liability under Environmental Laws, including without limitation, any liability to investigate, remediate, cleanup, monitor or take any similar actions with respect to the environmental condition of any property (whether owned or non-owned), facility or treatment, storage or disposal facility. None of the following exists or to Isis' or Ibis' Knowledge, has ever existed at the Real Property: underground storage tanks, septic tanks, asbestos containing materials, polychlorinated biphenyls, lead-based paint, urea-formaldehyde, dumps, landfills, or waste disposal areas, sumps, pits, lagoons, surface impoundments or wetlands, or any contamination of any kind of the surface, subsurface, groundwater or surface water. Ibis has not assumed or become subject to, whether expressly or by operation of Law, any liabilities of any other Person arising under Environmental Laws or pursuant to any type of agreement. The consummation of the transactions contemplated by this Master Agreement do not impose any obligation on the Business under any Environmental Law or require notification to or consent of any Governmental Authority or third party pursuant to any Environmental Law. Ibis has provided to AMI copies of all material environmental Licenses, reports, audits, assessments, and investigations, and any other material environmental documents, relating to Ibis or the Business to the extent the foregoing are in the possession, custody, or control of Isis or any of its Affiliates or Ibis.

(s) Offering Valid. Assuming the accuracy of the representations and warranties of AMI contained in Section 3.2 hereof, the offer, sale and issuance of the Shares (and the Additional Shares if AMI exercised the Subscription Right and acquired the Additional Shares pursuant to the Stock Subscription Agreement on the date hereof) will be exempt from the registration requirements of the Securities Act, and will have been registered or qualified (or are exempt from registration and qualification) under the registration, permit or qualification requirements of all applicable state securities Laws. Neither Ibis nor any agent on its behalf has

solicited or will solicit any offers to sell or has offered to sell or will offer to sell all or any part of the Shares or Additional Shares to any Person or Persons so as to bring the sale of such Shares or Additional Shares by Ibis within the registration provisions of the Securities Act or any state securities Laws.

(t) Financial Statements. Schedule 3.1(t) attached hereto contains the following financial statements (collectively the "Financial Statements"): (i) the profit and loss statement for the Division for the fiscal year ended December 31, 2006 and (ii) the profit and loss statement for Ibis and the related balance sheet (the "Most Recent Balance Sheet") for the nine month period ended September 30, 2007. The Financial Statements have been prepared in accordance with GAAP throughout the periods covered thereby, present fairly in all material respects the financial condition of Ibis or the Division (as the case may be) as of such dates and the results of operations of Ibis or the Division (as the case may be) for such periods, and are materially correct and complete and consistent with the books and records of Ibis (which books and records are materially correct and complete).

(u) Subsequent Events. Since the date of the Most Recent Balance Sheet, there has not been any material adverse change in the business, assets, liabilities, condition (financial or otherwise), operations, operating results, prospects, customer relations or supplier relations of Ibis and Ibis has and Isis has caused Ibis to conduct the Business in the ordinary course. Since the date of the Most Recent Balance Sheet:

(i) Ibis has not sold, leased, transferred, or assigned any of its assets to a third party, tangible or intangible, other than inventory in the ordinary course of business;

(ii) No party (including Ibis or Isis) has accelerated, terminated, modified, or canceled any material Contract (or series of related Contracts) to which Ibis is or was a party or by which the Business is or was bound;

(iii) Ibis has made capital expenditures consistent with its normal course of operations;

(iv) Ibis has not experienced any damage, destruction, or loss (whether or not covered by insurance) to its property over $50,000 in the aggregate;

(v) Ibis has not granted any increase in the base compensation of any employee, except in the ordinary course of business (including as to amount) or any bonus to, any employee, other than in the ordinary course of business;

(vi) Ibis has not amended, modified, or terminated any Plan;

(vii) Ibis has not entered into any transaction with any of its directors, officers, employees or Affiliates, except for transactions with its employees in the ordinary course of business;

(viii) Neither Ibis nor Isis has licensed, sublicensed, allowed any Encumbrance to exist on, abandoned, or permitted to lapse any Business IP or, except in

the ordinary course of business, disclosed any Confidential Information of Ibis or the Business to any Person (other than AMI and AMI's Representatives);

(ix) Ibis has not made a change in its accounting methods; and

(x) Ibis has not committed in any binding manner to any of the foregoing.

(v) Brokers' Fees. There are no brokerage commissions, finders' fees or similar compensation due in connection with the transactions contemplated by the Transaction Documents based on any arrangement or agreement made by or on behalf of Isis or Ibis. To the extent there are any brokerage commissions, finders' fees or similar compensation due in connection with the transactions contemplated by the Transaction Documents under [***] Isis shall be solely liable for any and all such amounts.

(w) Leased Real Property.

(i) Ibis does not own any real property and the ownership of any real property is not necessary for the operation of the Business. Ibis does not lease, sublease, license or otherwise grant any Person the right to use any real property. Neither Isis nor any of its Affiliates leases, subleases, licenses or occupies any real property used or occupied by, or necessary for the operation or conduct of, the Business.

(ii) Schedule 3.1(w)(ii) sets forth the names of the lessor and lessee, the address of each parcel of real property used by Ibis (collectively, the "Leased Real Property"), and a list of all leases, subleases, licenses and other agreements (whether written or oral) (collectively, "Leases") for each such Leased Real Property. None of the Leases is a ground lease. Ibis and Isis have delivered to AMI a true and complete copy of each such Lease document, and in the case of any oral Lease, a written summary of the material terms of such Lease. Ibis does not own any structures, improvements or fixtures located on any Leased Real Property (collectively, "Leasehold Improvements") and no Leasehold Improvements other than those provided to Ibis under the Corporate Services Agreement are material to the operation of the Business.

(iii) Each such Lease is legal, valid, binding, enforceable and in full force and effect.

(iv) Neither Ibis nor, to Isis' or Ibis' Knowledge, any other party to a Lease is in breach or default under such Lease, no event has occurred or circumstance exists which, with the delivery of notice, the passage of time or both, could reasonably be expected to constitute such a breach or default, or permit the termination, modification or acceleration of rent under such Lease and neither Ibis nor Isis has received notice that the Leased Real Property is in violation of any Applicable Law.

(v) No security deposit or portion thereof deposited with respect to such Lease has been applied in respect of a breach or default under such Lease which has not been redeposited in full. Neither Ibis nor any other Person owes any brokerage commissions, finder's fees, free rent or allowances with respect to such Lease.

(x) Contracts.

(i) Schedule 3.1(x)(i) lists the following Contracts relating to the Business or to which Ibis is a party: (A) Contract for the employment of any officer, individual employee, or other Person on a full-time, part-time, consulting, or other basis or Contract relating to loans to officers, directors, employees or Affiliates; (B) agreement or indenture relating to borrowed money or other Indebtedness or the mortgaging, pledging, or otherwise placing an Encumbrance on assets or Capital Stock of Ibis; (C) lease or agreement under which Ibis is the lessee of or holds or operates any property, real or personal, owned by any other party, except for any lease or agreement for real or personal property under which the aggregate annual consideration is less than or equal to $25,000; (D) lease or agreement under which Ibis is the lessor of or permits any Person to hold or operate any property, real or personal, owned or controlled by Ibis; (E) distribution or franchise agreement; (F) agreement with a term of more than six months and (1) which is not terminable by Ibis upon less than 90 days' notice without penalty or (2) which involves aggregate annual consideration in excess of $25,000; (G) agreements relating to ownership of or investments in any business or enterprise, including joint ventures and minority equity investments; (H) Contract prohibiting it from freely engaging in any business or competing anywhere in the world; (I) except as otherwise disclosed on Schedule 3.1(x)(i) any other Contract or group of related Contracts with the same party or group of affiliated parties that involves aggregate annual consideration from or to Ibis in excess of $100,000; or (J) any Contract that is otherwise material to Ibis and/or the Business, including, without limitation, any IP Contract or Government Contract, whether or not entered into in the ordinary course of business and whether or not performance thereunder has been completed. All of the Contracts and other similar arrangements set forth on or required to be set forth on Schedule 3.1(x)(i) (the "Ibis Contracts").

(ii) All of the Ibis Contracts are valid, binding, enforceable and in full force and effect, and the Financing will not cause such Contracts to cease to be valid, binding, enforceable and in full force and effect on identical terms following the Closing Date. Each of Isis or Ibis, as applicable, and, to Isis' or Ibis' Knowledge, each counterparty thereto has performed all material obligations required to be performed by it and is not in default under or in breach of or in receipt of any claim of default or breach under any Ibis Contract. No event has occurred which with the passage of time or the giving of notice or both would result in a default, breach or event of noncompliance by either Ibis or Isis or, to Isis' or Ibis' Knowledge, any other party under any such Ibis Contract. Neither Isis nor Ibis has received notice of the intention of any party to cancel or terminate any Ibis Contract and, to Isis' or Ibis' Knowledge, there has not been any breach or anticipated breach by the other parties to any such Ibis Contract.

(iii) Isis has provided AMI with a true and correct copy of all Ibis Contracts in each case together with all amendments, waivers, or other changes thereto (all of which are disclosed on Schedule 3.1(x)(i)). Schedule 3.1(x)(i) contains an accurate and complete description of all material terms of all oral Contracts referred to therein.

(y) Insurance. Schedule 3.1(y) attached hereto lists and briefly describes each insurance policy maintained by Ibis or Isis with respect to the Business (the "Insurance Policies"), together with a claims history for the past five (5) years for Ibis and, with respect to the Business, Isis. All of the Insurance Policies are in full force and effect, and neither Ibis nor Isis with respect to the Business is in default with respect to its obligations under any such insurance policy and neither Ibis nor Isis, with respect to the Business has been denied insurance coverage. Neither Ibis nor Isis, with respect to the Business has any self-insurance or co-insurance programs.

(z) Customers and Suppliers. Schedule 3.1(z) accurately sets forth a list of the Business' top ten customers by revenue for the fiscal year ended December 31, 2006 and the nine month period ended September 30, 2007. Except as set forth on Schedule 3.1(z), neither Isis nor Ibis has received any indication from any material customer of the Business or any Governmental Authority to the effect that, and neither Isis nor Ibis has any reason to believe that, such customer or Governmental Authority will in the future stop, or materially decrease the rate of buying products or services from the Business. Schedule 3.1(z) also accurately sets forth a list of the Business' top ten suppliers by dollar amount for the nine month period ended September 30, 2007. Except as set forth on Schedule 3.1(z), neither Isis nor Ibis has received any indication from any material supplier of the Business to the effect that, and neither Isis nor Ibis has any reason to believe that, such supplier will stop or materially decrease the rate of providing products or services to the Business and its customers. Neither Isis nor Ibis is involved in any material dispute with any customer or supplier of or to the Business.

(aa) No Material Adverse Effect. Since September 30, 2007, there has been no Material Adverse Effect.

(bb) Names and Locations. During the five-year period prior to the date hereof, neither Ibis nor the Business has used any name or names under which it has invoiced account debtors or maintained records concerning the assets used in the operation of the Business, other than Ibis Biosciences, Inc. and all of the assets used in the operation of the Business are located at the Leased Real Property.

(cc) Directors, Officers and Bank Accounts. Schedule 3.1(cc) (i) sets forth a true and correct list of the directors and officers of Ibis and the title of each such officer. Schedule 3.1(cc) (ii) lists all of Ibis' bank accounts, safety deposit boxes and lock boxes (designating each authorized signatory with respect thereto).

(dd) Regulatory Filings. Ibis and Isis have made available for inspection by AMI all material registrations, filings or submissions made with any Regulatory Authority or the SEC, and reports of audits ever issued by any Governmental Authority made by or with respect to Ibis or the Business. Ibis or Isis has timely filed, or caused to be timely filed, all material reports, statements, documents, registrations, filings or submissions required to be filed by Ibis or the Business with any Governmental Authority in connection with the operation of Ibis or the Business. All such registrations, filings and submissions are in material compliance in all respects with all Laws when filed or as amended or supplemented, and no deficiencies have been asserted by any such Governmental Authority with respect to such registrations, filings or submissions.

(ee) Disclosure. None of the Investment Documents, nor any of the Schedules delivered in connection herewith or therewith, contains any untrue statement of a material fact or omits a material fact necessary to make the statements contained herein or therein, in light of the circumstances in which they were made, not misleading. To Isis' or Ibis' Knowledge, there is no event, circumstance or other fact which Isis or Ibis has not disclosed to AMI in writing which has had or would reasonably be expected to have a Material Adverse Effect.

3.2 Representations and Warranties of AMI. AMI hereby represents and warrants to Ibis and Isis as follows (provided that such representations and warranties do not lessen or obviate the representations and warranties of Ibis and Isis set forth in this Master Agreement):

(a) Power and Authority. AMI has the power, authority and the legal right to enter into this Master Agreement, the Call Option Agreement and the Investor Rights Agreement and to perform its obligations hereunder and thereunder, and it has taken all necessary action required to authorize the execution and delivery of each such agreement and the performance of its obligations hereunder and thereunder.

(b) Enforceability. Each of this Master Agreement, the Call Option Agreement and the Investor Rights Agreement has been duly executed and delivered on behalf of AMI and constitutes its legal, valid and binding obligation and is enforceable against it in accordance with its terms subject to the effects of bankruptcy, insolvency or other Laws of general application affecting the enforcement of creditor rights.

(c) Governmental Authority; Consents. All necessary consents, approvals and authorizations of all Governmental Authorities and other parties required to be obtained by AMI in connection with the execution and delivery of this Master Agreement, the Call Option Agreement and the Investor Rights Agreement and the performance of its obligations hereunder and thereunder have been obtained.

(d) No Conflicts. The execution and delivery of this Master Agreement, the Call Option Agreement and the Investor Rights Agreement by AMI and the performance of its obligations hereunder and thereunder (i) do not conflict with or violate any requirement of Applicable Law or any provision of its certificate of incorporation or bylaws and (ii) do not require any notice, conflict with, violate, or breach or constitute a default or require any consent not already obtained or give rise to any termination or acceleration right under, any contractual obligation by which such Party is bound.

(e) Due Organization; Qualification. AMI is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, with full corporate power and authority to enter into this Master Agreement, the Call Option Agreement and the Investor Rights Agreement and to perform its obligations hereunder and thereunder.

(f) Investment Representations. AMI understands that the Shares have not been registered under the Securities Act. AMI also understands that the Shares are being

offered and sold pursuant to an exemption from registration contained in the Securities Act based in part upon AMI's representations contained in this Master Agreement. AMI hereby represents and warrants as follows:

(i) *AMI Bears Economic Risk.* AMI may be required to bear the economic risk of its investment in the Shares indefinitely unless the Shares are registered pursuant to the Securities Act, or an exemption from registration is available. AMI understands that Ibis has no present intention of registering the Shares or any shares of its Capital Stock. AMI also understands that there is no assurance that any exemption from registration under the Securities Act will be available and that, even if available, such exemption may not allow AMI to Transfer all or any portion of the Shares under the circumstances, in the amounts or at the times AMI might propose.

(ii) *Acquisition for Own Account.* AMI is acquiring the Shares for AMI's own account for investment only, and not with a view towards their distribution.

(iii) *Accredited Investor.* AMI represents that it is an accredited investor within the meaning of Regulation D under the Securities Act.

(iv) *Ibis Information.* Ibis and Isis have given AMI an opportunity to discuss Ibis' business, management and financial affairs with directors, officers and management of Ibis and AMI has had an opportunity to review Ibis' operations and facilities.

(v) *Rule 144.* AMI acknowledges and agrees that the Shares are "restricted securities" as defined in Rule 144 promulgated under the Securities Act as in effect from time to time and must be held indefinitely unless they are subsequently registered under the Securities Act or an exemption from such registration is available. AMI has been advised or is aware of the provisions of Rule 144, which permits limited resale of shares purchased in a private placement subject to the satisfaction of certain conditions, including, among other things: the availability of certain current public information about Ibis, the resale occurring following the required holding period under Rule 144 and the number of shares being sold during any three-month period not exceeding specified limitations.

(g) Transfer Restrictions. AMI acknowledges and agrees that the Shares are subject to restrictions on Transfer as set forth in the Investor Rights Agreement.

(h) Legends. AMI understands and agrees that the certificates evidencing the Shares, or any other Capital Stock issued in respect of the Shares upon any stock split, stock dividend, recapitalization, merger, consolidation or similar event, will bear the legends required by the Investor Rights Agreement, including legends relating to restrictions on Transfer under federal and state securities Laws and legends required under applicable state securities Laws.

SECTION 4. [RESERVED.]

SECTION 5. CONFIDENTIALITY; NOTICE OF DEVELOPMENTS.

5.1 Disclosure and Use Restriction. Each Party agrees that for a period of three (3) years after the date hereof, a Party (the "Receiving Party") receiving or that has received Confidential Information of the other Party (the "Disclosing Party") will (a) maintain and cause its Representatives to maintain in confidence such Confidential Information using not less than the efforts such Receiving Party uses to maintain in confidence other proprietary information of similar kind and value, (b) not disclose such Confidential Information except to the Receiving Party's employees or Affiliates having a need-to-know such Confidential Information solely for purposes of performing the Receiving Party's obligations under the Investment Documents, (c) not disclose such Confidential Information to any Person without the prior written consent of the Disclosing Party, except for disclosures expressly permitted by the Investment Documents, and (d) not use such Confidential Information for any purpose except those expressly permitted by the Investment Documents. Notwithstanding the foregoing, the provisions of this Section 5.1, Section 5.2 and Section 5.3 shall terminate and be of no further force or effect from and after the Acquisition Closing. The Letter Agreement by and between Isis and Abbott, dated as of November 8, 2007 shall terminate and be of no further force and effect upon the Financing Closing; *provided* that any Confidential Information of any Party disclosed prior to the Financing Closing shall be governed by the terms hereof. Upon AMI's request Isis will return or destroy (and certify to AMI any such destruction) all Confidential Information of AMI or its Affiliates and upon Isis' request, AMI will return or destroy (and certify to Isis any such destruction) all Confidential Information of Isis that is not Confidential Information of Ibis; *provided*, that AMI may retain one (1) copy of Isis' Confidential Information in Abbott's confidential files. In addition, after the expiration of the Call Period, upon Isis' or Ibis' written request, AMI will return or destroy (and certify to Isis and Ibis any such return or destruction) all Confidential Information of Ibis; *provided*, that AMI may retain one (1) copy of Ibis' Confidential Information in Abbott's confidential files.

5.2 Authorized Disclosure. To the extent (and only to the extent) that it is reasonably necessary, a Party may disclose Confidential Information belonging to the other Party in the following instances:

(a) defending litigation related to the Confidential Information to be disclosed;

(b) complying with Applicable Laws (including, without limitation, the rules and regulations of the SEC or any national securities exchange, and compliance with Tax Laws) and with judicial process; and

(c) disclosure, in connection with the performance of the Investment Documents and solely on a need-to-know basis, to employees or independent contractors (including without limitation consultants and clinical investigators), each of whom prior to disclosure must be bound by written obligations of confidentiality and non-use no less restrictive than the obligations set forth in Section 5.1, this Section 5.2 and Section 5.3; *provided*, that the Receiving Party will remain responsible for any failure by any Person who receives Confidential

Information pursuant to this Section 5.2 to treat such Confidential Information as required under Section 5.1, this Section 5.2 and Section 5.3.

5.3 Effect of Authorized Disclosure. If and whenever any Confidential Information is disclosed in accordance with Section 5.2, such disclosure will not cause any such information to cease to be Confidential Information except to the extent that such permitted disclosure results in a public disclosure of such information (other than by breach of this Master Agreement). Except as prohibited by Law, the Receiving Party will notify the Disclosing Party of the Receiving Party's intent to make such disclosure pursuant to clauses (a) or (b) of Section 5.2 sufficiently prior to making such disclosure so as to allow the Disclosing Party adequate time to take whatever action the Disclosing Party may deem appropriate to protect the confidentiality of the information. In addition, in the event any Party proposes to file with any Governmental Authority a Transaction Document including, without limitation, as an exhibit to a registration statement, periodic report, or current report, the Party proposing to make such filing will notify the other Parties of such intention and will work in good faith with the other Parties to obtain confidential treatment of any material terms of the Transaction Documents that such other Parties request be kept confidential (except to the extent advised by counsel or such Governmental Authority that confidential treatment is not available for such information).

5.4 Terms of Agreement. The existence and the terms and conditions of the Transaction Documents that the Parties have not specifically agreed to disclose pursuant to Section 5.2 or Section 5.7 will be considered Confidential Information of both Parties. AMI and, subject to the terms of Section 5.5, Isis may disclose such terms to a bona fide potential investor, investment banker, acquirer, merger partner or other potential business partner of AMI or Isis, respectively, and their attorneys and agents, *provided* that each such Person to whom such information is to be disclosed is informed of the confidential nature of such information and has entered into a written agreement with the Party requiring such Person to keep such information confidential.

5.5 Exclusivity. During the Call Period or, if AMI exercises the Call Option, until the Acquisition Closing, neither Isis nor Ibis nor any of their respective Affiliates shall (and each shall (i) cause its Representatives and (ii) instruct its investment bankers, attorneys and accountants not to), directly or indirectly, encourage, solicit, approve or recommend or participate in or initiate discussions or negotiations with, or provide any information to, any Person or group (other than AMI and its Representatives) concerning any Purchase Offer.

Isis shall promptly, but in any event within [***] [***], notify AMI of the existence of any [***] received by Ibis or Isis or their respective Representatives regarding any [***] and Ibis and Isis shall promptly, but in any event within [***], communicate to AMI the [***] which they may receive (and will immediately provide to AMI [***]. Ibis and Isis shall promptly provide to AMI any non-public information provided to any other Person by or on behalf of Ibis or Isis in connection with [***].

5.6 Injunctive Relief. The Parties hereto understand and agree that remedies at Law may be inadequate to protect against any breach of any of the provisions of this Section 5 by either Party or their employees, agents, officers or directors or any other person acting in concert with it or on its behalf. Accordingly, each Party may be entitled to seek injunctive relief by a court of competent jurisdiction against any action that constitutes any such breach of this Section 5.

5.7 Press Release; Public Disclosure**.** Upon execution of this Master Agreement, Isis will issue the mutually agreed upon press release, attached hereto as Exhibit E, announcing the consummation of the transactions contemplated hereby. Each Party agrees not to issue any other press release or other public statement relating to or make any public filing with respect to the Transaction Documents or the transactions contemplated hereby without the prior written consent of the other Party, which consent will not be unreasonably withheld or delayed. Each Party agrees to provide to the other Party a copy of any public announcement or public filing regarding the Transaction Documents or the subject matter thereof as far in advance as practicable under the circumstances prior to its scheduled release. Except under extraordinary circumstances, each Party will provide the other with an advance copy of any such announcement at least [***] prior to its scheduled release. The contents of any announcement or filing or similar publicity which has been reviewed, approved and released by the reviewing Party may be re-released by either Party without a requirement for advance notice or re-approval.

5.8 Notice of Developments. During the Call Period, Isis shall promptly (once Isis or Ibis obtains Knowledge thereof), but in any event within [***] of such Knowledge, inform AMI in writing of:

(i) any Material Adverse Effect;

(ii) any material inaccuracy in or breach of any representation or warranty of Ibis or Isis made herein which Isis or Ibis acquire Knowledge of after the date hereof.

No such disclosure by Ibis or Isis pursuant to this Section 5.8, however, shall be deemed to limit or otherwise affect the liability of Ibis and Isis under Section 7.2(a).

SECTION 6. [RESERVED.]

SECTION 7. ADDITIONAL AGREEMENTS.

7.1 Survival. Except as expressly provided otherwise herein, the covenants in this Master Agreement shall survive the Financing Closing indefinitely. The representations and warranties in this Master Agreement shall survive the Financing Closing as follows:

(a) the Fundamental Isis Representations and Fundamental AMI Representations shall terminate on [***];

(b) the representations and warranties in Section 3.1(l) (Intellectual Property) shall terminate on the earlier of (i) the [***]-year anniversary of the Closing Date and (ii) the Acquisition Closing; and

(c) all other representations and warranties in this Master Agreement shall terminate on the earlier of (i) the [***]-year anniversary of the Closing Date and (ii) the Acquisition Closing.

Notwithstanding the foregoing, claims for indemnification pursuant to Section 7.2 as to which the Indemnified Party has given the Indemnifying Party proper notice pursuant to Section 8.8 prior to the expiration of the applicable survival period shall survive such expiration until such claims are resolved by written agreement of the Parties or by order of a court of competent jurisdiction.

7.2 Indemnification.

(a) Ibis and Isis shall jointly and severally indemnify, defend and hold harmless AMI, its officers, directors, shareholders, employees, representatives, agents and Affiliates (collectively, the "AMI Group") against any Losses which any of them may suffer, sustain, or become subject to, as a result of:

(i) the breach of any representation or warranty made by Ibis or Isis in the Investment Documents or in any certificate delivered by Isis or Ibis pursuant hereto or thereto; and

(ii) the breach of any covenant or agreement made by Ibis or Isis in the Investment Documents or in any certificate delivered by Isis or Ibis pursuant hereto or thereto.

(b) AMI shall indemnify, defend and hold harmless Ibis and Isis, their respective officers, directors, shareholders, employees and Affiliates (the "Seller Group") against any Losses which any of them may suffer, sustain or become subject to, as the result of:

(iii) the breach of any representation or warranty made by AMI in the Investment Documents or in any certificate delivered by AMI pursuant hereto or thereto; and

(iv) the breach of any covenant or agreement made by AMI in the Investment Documents or in any certificate delivered by AMI pursuant hereto or thereto.

(c) If any third party shall notify any Party to this Master Agreement (the "Indemnified Party") of any matter which may give rise to a claim (a "Third Party Claim") for indemnification against any other Party to this Master Agreement (the "Indemnifying Party") under this Section 7.2, then the Indemnified Party shall notify the Indemnifying Party thereof; provided that the failure to so notify the Indemnifying Party shall not relieve the Indemnifying Party of its obligations hereunder except to the extent such failure shall have actually materially prejudiced the Indemnifying Party. Once the Indemnified Party has given notice of the matter to the Indemnifying Party, the Indemnified Party shall defend against the matter in any manner it reasonably may deem appropriate. Notwithstanding anything herein to the contrary, the Indemnifying Party shall not have the right to participate in such defense if the claim in which the Indemnifying Party seeks to participate (i) seeks non-monetary relief that does not seek to obtain a license or other access to, restrict the scope of, or adversely affect the enforceability of, any Business IP or Intellectual Property controlled by the Indemnifying Party, (ii) involves criminal allegations against an Indemnified Party or (iii) is one in which the Indemnifying Party is also a party and joint representation would be inappropriate or there may be legal defenses

available to the Indemnified Party which are different from or additional to those available to the Indemnifying Party. The Indemnifying Party may, at its sole cost and expense, participate in the defense of such Claim with co-counsel of its choice. The Indemnified Party will not consent to the entry of any judgment with respect to the matter or enter into any settlement with respect to the matter without the Indemnifying Party's prior written consent (not to be unreasonably withheld, conditioned or delayed).

(d) None of the AMI Group or the Seller Group shall be entitled to recover any Losses relating to any matter arising under one provision of this Master Agreement to the extent that any such Person has already recovered Losses with respect to such matter pursuant to other provisions of this Master Agreement or the Acquisition Agreement.

(e) In determining the amount of any Loss arising from the breach of any representation, warranty, covenant or agreement hereunder, any materiality, Material Adverse Effect, or similar qualification contained therein shall be disregarded.

(f) Indemnification for each Loss for which an Indemnifying Party, but for this Section 7.2(f), would be liable under Section 7.2(a) or Section 7.2(b) shall be reduced by the amount of any insurance proceeds actually paid to any member of the AMI Group or the Seller Group, as the case may be, by any unaffiliated third party with respect to such Loss, in each case net of any Losses incurred by any member of the AMI Group or the Seller Group as the case may be in collecting such proceeds or payments; *provided* that this Section 7.2(f) shall not limit in any respect the right of any member of the AMI Group or the Seller Group, as the case may be, to pursue indemnification from an Indemnifying Party hereunder or from recovering for any Loss not reduced to zero pursuant to this Section 7.2(f). Nothing contained herein shall be deemed to cause any amounts for which a member of the AMI Group or the Seller Group, as the case may be, would ultimately be responsible, as a result of deductibles, self-insurance, indemnification of insurers, caps or similar items or arrangements, to not be subject to indemnification as "Losses" hereunder.

(g) For Tax purposes, the parties agree to treat all payments made under this Section 7.2 as adjustments to the Share Purchase Price.

7.3 Affirmative Covenants of Ibis and Isis.

(a) Due Diligence. During the Call Period or, if AMI exercises the Call Option, until the Acquisition Closing (i) AMI shall have the right to conduct a legal, business, operational and financial review of the Business in accordance with a reasonable procedure to be agreed upon by the Parties in good faith and designed to limit disruptions to the operations of Ibis and Isis and (ii) Ibis and Isis shall cooperate with AMI in performing such review, including, without limitation, providing reasonable access to its records, Representatives and properties during normal business hours; *provided* that Isis and Ibis may limit AMI's access with respect to each of the foregoing to the extent necessary to comply with Applicable Law.

(b) Ordinary Course. As long as AMI or any of its Affiliates hold at least [***] Shares or Additional Shares (subject to adjustment for any stock dividends, combinations, splits, recapitalization and the like with respect to such Shares or Additional Shares after the

issuance thereof), Ibis shall and Isis shall cause Ibis to (i) conduct the Business only in the ordinary course (ii) use commercially reasonable efforts to keep Ibis' business organization and properties intact, including Ibis' business operations, physical facilities, working conditions, executives and key employees and Ibis' and the Business' relationships with consultants, independent contractors, lessors, licensors, suppliers, customers, carriers, and others having business relations with Ibis or the Business (iii) use commercially reasonable efforts to keep in full force and effect and maintain in good repair, order and condition, Ibis' organizational existence and all of its and the Business' assets, Contracts, rights, franchises, and Business IP and use commercially reasonable efforts to cause Ibis' and the Business' current insurance (or reinsurance) policies not to be canceled or terminated or any of the coverage thereunder to lapse. Notwithstanding anything in the foregoing to the contrary, nothing in this Section 7.3(b) shall (A) prohibit or limit an Initial Offering, (B) after the Call Option Expiration Date, prohibit or limit a Change of Control of Ibis in compliance with the terms of the Investor Rights Agreement or (C) require any additional investment by Isis in Ibis.

(c) Consolidation of Ibis and Isis. Unless the provisions of the Code pertaining to filing Tax Returns as a consolidated group are amended prior to the Acquisition Closing, Ibis and Isis will file a consolidated Tax Return in lieu of separate Tax Returns with respect to income Tax imposed by Chapter 1 of the Code for the Tax year beginning January 1, 2007 through and including the Acquisition Closing. In the event of an Internal Revenue Service audit of Isis arising out or related to the consolidation of Ibis and Isis in such consolidated Tax Return, Isis will promptly (but in any event within [***] [***]) notify AMI of such audit and allow AMI to participate and advise Ibis and Isis in connection with such audit. Upon the Acquisition Closing, this provision will be superseded by Section 8.12 of the Acquisition Agreement.

7.4 Negative Covenants of Ibis and Isis. Until the earlier of (i) the expiration of the Call Period and (ii) the execution of the Acquisition Agreement, Ibis shall not and, with respect to Ibis and the Business, Isis shall not and shall cause Ibis not to:

(a) amend or waive any provision of Ibis' Certificate of Incorporation;

(b) take any action that would reasonably be expected to adversely affect the rights, preferences or privileges of the Shares or Additional Shares;

(c) take any action by written stockholder consent of Ibis without at least [***] prior written notice to AMI;

(d) redeem, repurchase, pay or declare dividends or other distributions with respect to any Capital Stock of Ibis;

(e) issue any Capital Stock of Ibis or any rights to acquire Capital Stock of Ibis;

(f) authorize or designate, whether by reclassification or otherwise, any new class or series of Capital Stock of Ibis or any increase in the authorized or designated number of any class or series of Capital Stock of Ibis;

(g) enter into any transaction of merger, consolidation or sale of control, or liquidate, reorganize, recapitalize, wind up or dissolve Ibis, or transfer any portion of Ibis' properties, assets or business other than transfers of inventory in the ordinary course of business;

(h) sell, transfer, assign, license or sublicense, or allow any Encumbrance on any Business IP other than (i) rights of the U.S. federal government in Intellectual Property pursuant to the Government Contracts set forth on Schedule 3.1(l)(iii) or new Government Contracts entered into in the ordinary course of business and (ii) end user license agreements related to the Software embodied in the T5000 Biosensor Systems that are issued in the ordinary course of business solely to purchasers of T5000 Biosensor Systems;

(i) abandon or permit to lapse any Business IP other than patents expiring at the end of their statutory terms (and not as a result of any act or omission by either Ibis or Isis, including, without limitation, a failure to pay any required maintenance fees) and limitations to the scope of claims of any pending patent application made during the ordinary course of prosecuting such pending patent applications;

(j) disclose any Confidential Information of the Business to any Person (other than AMI and its Representatives) other than in the ordinary course of business;

(k) create, incur, guarantee, assume, or be liable for any Indebtedness, other than Permitted Indebtedness in the ordinary course of business;

(l) subject any tangible asset of the Business to any Encumbrance, other than Permitted Encumbrances in the ordinary course of business and rights of the U.S. federal government in certain equipment purchased using government funds pursuant to (i) the Government Contracts set forth on Schedule 3.1(l)(iii) or (ii) new Government Contracts entered into in the ordinary course of business;

(m) (i) make any loan to or enter into any transaction with any officer, employee, partner or Affiliate, (ii) increase any officer's, employee's or partner's compensation outside the ordinary course of business, (iii) increase or accelerate any benefit, vesting schedule, obligation, subsidy or similar feature under any Plan outside the ordinary course of business, (iv) establish any Plan (except for the Permitted Employee Compensation Plan as contemplated by this Master Agreement), (v) amend any Plan outside the ordinary course of business or commence making contributions to any multiemployer plan, or (vi) cause the number of full-time equivalent employees of Ibis (not including temporary employees) to exceed [***] in the aggregate or to be less than [***] in the aggregate;

(n) make any acquisition, by means of merger, consolidation or otherwise, or any disposition, of assets or Capital Stock of any other Person;

(o) make any loans or capital contributions to, or investments in, any other Person, except advances to employees for reasonable expenses incurred in the ordinary course of business;

(p) enter into any strategic alliance or joint venture;

(q) enter into any joint marketing arrangement or agreement outside the ordinary course of business;

(r) materially delay or defer maintenance or repairs on any of Ibis' assets;

(s) waive or release any material Claim of Ibis;

(t) increase or decrease marketing or promotional spending in any material respect from the rates established in the anticipated 2008 Budget;

(u) except as otherwise contemplated by this Agreement, pay, discharge, settle or satisfy any Claim, liability or obligation or litigation (whether or not commenced prior to the date of this Agreement) outside the ordinary course of business;

(v) take any other action which would reasonably be expected to interfere with, impede or materially delay the transactions contemplated by the Transaction Documents or dilute the benefits thereof to AMI and its Affiliates; or

(w) commit, or enter into any agreement to do, any of the foregoing.

7.5 No Solicitation of AMI Employees. Until (a) the execution of the Acquisition Agreement (it being understood that if the Acquisition Closing does not occur, then until the date provided for in clause (b)) or (b) if the Call Option expires or terminates, the date that is [***] years following the Call Option Expiration Date (the applicable period, the "Nonsolicitation Period"), neither Isis nor Ibis shall and neither shall permit any of their respective Representatives to directly or indirectly (i) without the prior written consent of AMI, induce or attempt to induce any employee of AMI or any member of the Abbott Transaction Team to leave the employ of AMI or the applicable Abbott Affiliate, or in any way interfere with the relationship between AMI or the applicable Abbott Affiliates and any employee of AMI or any member of the Abbott Transaction Team, or Known consultant or independent contractor thereof or (ii) without the prior written consent of AMI, hire directly or through another entity any employee of AMI or any member of the Abbott Transaction Team or any Person who was an employee of AMI or a member of the Abbott Transaction Team who was employed by Abbott or any of its Affiliates during the [***] months prior to the date of such hiring, in each case to work for Isis or Ibis.

7.6 No Solicitation of Ibis or Isis Employees. During the Nonsolicitation Period, AMI and its Affiliates will cause AMI and the members of the Abbott Transaction Team not to, directly or indirectly, (i) without the prior written consent of Isis or Ibis (as the case may be), induce or attempt to induce any employee of Isis or Ibis to leave the employ of Isis or Ibis, or in any way interfere with the relationship between Isis or Ibis and any of their respective employees, or Known consultant or independent contractor thereof or (ii) without the prior written consent of Isis or Ibis (as the case may be), hire directly or through another entity any employee of Isis or Ibis or any Person who was an employee of Isis or Ibis who was employed by Isis or Ibis during the [***] months prior to the date of such hiring, in each case to work for AMI.

7.7 No Solicitation of Ibis Employees. During the Call Period, Isis shall not and shall not permit any of its Representatives to directly or indirectly (i) without the prior written consent of AMI, induce or attempt to induce any employee of Ibis to leave the employ of Ibis, or in any way interfere with the relationship between Ibis and any employee, consultant or independent contractor thereof, or (ii) without the prior written consent of AMI, hire directly or through another entity any employee of Ibis or any Person who was an employee of Ibis during the [***] months prior to the date of such hiring.

For purposes of Sections 7.5, 7.6 and 7.7, "recruit," "solicit" or "induce" shall not be deemed to mean (i) circumstances where an employee, consultant or independent contractor or former employee, consultant or independent contractor initiates contact with a Party with regard to possible employment, or (ii) general solicitations of employment not specifically targeted at specific employees of a Party, including responses to general advertisements.

Notwithstanding anything in Sections 7.5, 7.6 or 7.7, to the contrary, if at any time a court holds that the restrictions stated in Sections 7.5, 7.6 or 7.7 or any part of any of the foregoing are unreasonable or otherwise unenforceable under circumstances then existing, the Parties hereby agree that the maximum period, scope or geographical area determined to be reasonable under such circumstances by such court will be substituted for the stated period, scope or area. The Parties acknowledge and agree that money damages may not be an adequate remedy for any breach or threatened breach of the provisions of Sections 7.5, 7.6 or 7.7 and that, in such event, any Party or its successors or assigns may, in addition to any other rights and remedies existing in its or their favor, apply to any court of competent jurisdiction for specific performance, injunctive and/or other relief in order to enforce or prevent any violations of the provisions of Sections 7.5, 7.6 or 7.7 (including, if the court so determines, the extension of the Nonsolicitation Period by a period equal to the length of court proceedings necessary to stop such violation). Any injunction shall be available without the posting of any bond or other security. In the event of an alleged breach or violation by any Party or any of their respective Representatives of any of the provisions of Sections 7.5, 7.6 or 7.7, the Nonsolicitation Period will be tolled until such alleged breach or violation is resolved. The Parties agree that the restrictions contained in Sections 7.5, 7.6 and 7.7 are reasonable in all respects.

SECTION 8. MISCELLANEOUS.

8.1 Governing Law; Alternative Dispute Resolution Procedure. This Master Agreement will be governed by and construed under the laws of the State of Delaware in all respects, without giving effect to any conflict of law principles thereof. The Parties recognize that from time to time a dispute may arise relating to a Party's rights or obligations under this Master Agreement or the other Transaction Documents. The Parties agree that any such dispute shall be resolved by the Alternative Dispute Resolution ("ADR") provisions set forth in Exhibit D the result of which shall be binding upon the Parties.

8.2 Successors and Assigns. No Party may assign either this Agreement or any of its rights, interests or obligations hereunder without the prior written approval of the other Parties; *provided* that (i) AMI may (x) assign any or all of its rights and interests hereunder to one or more of its Affiliates, (y) designate one or more of its Affiliates to perform its obligations hereunder (in any or all of which cases AMI nonetheless shall remain responsible for the

performance of all of its obligations hereunder), and (z) assign any or all of its rights and interests hereunder in connection with a Change of Control of AMI and (ii) Isis may assign its rights and obligations in connection with a Change of Control of Isis if such Transfer involves all of the Capital Stock of Ibis that is owned by Isis and the surviving or acquiring entity assumes all of Isis' obligations under the Investment Documents. Except as otherwise expressly provided herein, the provisions hereof shall inure to the benefit of, and be binding upon and be enforceable by the Parties and their respective successors, assigns, heirs, executors and administrators.

8.3 Entire Agreement; Exhibits and Schedules.

(a) This Master Agreement, the Exhibits and Schedules hereto, the Transaction Documents and the other documents delivered pursuant hereto or referred to herein constitute the full and entire understanding and agreement between the Parties with regard to the subject hereof and no party will be liable for or bound to any other in any manner by any oral or written representations, warranties, covenants and agreements except as specifically set forth herein or therein.

(b) The Exhibits and Schedules identified in this Agreement are incorporated herein by reference and made a part hereof. The Parties acknowledge and agree that (i) the Disclosure Schedules are arranged in sections corresponding to the sections and paragraphs of this Master Agreement and shall qualify the specifically referenced corresponding representations and warranties of the Parties contained in this Agreement, (ii) to the extent this Master Agreement requires disclosure of any matter, such matter disclosed pursuant to one provision, subprovision, section or subsection of the Disclosure Schedules shall be deemed disclosed only to the extent actually disclosed with respect to the specific provision, subprovision, section or subsection of the Disclosure Schedule that it is actually disclosed pursuant to; and (iii) section numbers and titles inserted in the Disclosure Schedules are for convenience of reference only and shall to no extent have the effect of amending or changing the express description of such sections of the Disclosure Schedules as set forth in this Master Agreement. Information set forth in each section of the Disclosure Schedules specifically refers to the section of this Master Agreement to which such information is responsive, and such information shall not be deemed to have been disclosed with respect to any statement made in any other section of this Master Agreement. Any capitalized terms used in any Schedule but not otherwise defined therein shall have the meanings ascribed to such terms in this Master Agreement.

8.4 No Third Party Beneficiaries. This Master Agreement shall not confer any rights or remedies upon any Person other than the Parties and their respective successors and permitted assigns.

8.5 Severability. In the event that any provision of this Agreement, or the application thereof, becomes or is declared by a court of competent jurisdiction to be illegal, void or unenforceable, the remainder of this Agreement shall continue in full force and effect and the application of such provision to other Persons or circumstances shall be interpreted so as reasonably to effect the intent of the Parties hereto. The Parties further agree to replace such void or unenforceable provision of this Agreement with a valid and enforceable provision that will achieve, to the extent possible, the economic, business and other purposes of such void or unenforceable provision.

8.6 Amendment and Waiver. This Master Agreement may be amended or modified, and the rights and obligations of the Parties under this Master Agreement may be waived, only upon the written consent of each Party. The other Investment Documents may only be amended as specifically set forth therein.

8.7 Delays or Omissions. It is agreed that no delay or omission to exercise any right, power or remedy accruing to any Party, upon any breach, default or noncompliance by another Party under an Investment Document or Ibis' Certificate of Incorporation, will impair any such right, power or remedy, nor will it be construed to be a waiver of any such breach, default or noncompliance, or any acquiescence therein, or of or in any similar breach, default or noncompliance thereafter occurring. It is further agreed that any waiver, permit, consent or approval of any kind or character on any Party's part of any breach, default or noncompliance under an Investment Document or Ibis' Certificate of Incorporation or any waiver on such Party's part of any provisions or conditions of an Investment Document, or Ibis' Certificate of Incorporation must be in writing and will be effective only to the extent specifically set forth in such writing. All remedies, either under an Investment Document, Ibis' Certificate of Incorporation, bylaw, or otherwise afforded to any Party, will be cumulative and not alternative.

8.8 Notices. All notices or other communications that are required or permitted under an Investment Document will be in writing and delivered personally with acknowledgement of receipt, sent by facsimile (and promptly confirmed by personal delivery, registered or certified mail or overnight courier as provided herein), sent by nationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, addressed as follows:

If to Ibis, to:

Ibis Biosciences Inc.
1896 Rutherford Road
Carlsbad, CA 92008
Attention: President
Facsimile: (760) 603-4653

If to Isis, to:

Isis Pharmaceuticals, Inc.
1896 Rutherford Road

Carlsbad, CA 92008
Attention: Chief Financial Officer
Facsimile: (760) 603-4650

with a copy to:

Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008
Attention: General Counsel
Facsimile: (760) 268-4922

If to AMI, to:

Abbott Laboratories
Corporate Transactions and Medical Products Legal Operations
Dept. 322, Bldg. AP6A
100 Abbott Park Road
Abbott Park, IL 60064-6010
Attention: Vice President and Associate General Counsel
Facsimile: (847) 938-1206

with a copy to:

Kirkland & Ellis LLP
200 East Randolph Drive
Chicago, IL 60601
Attention: R. Scott Falk, P.C.
R. Henry Kleeman
Facsimile: (312) 861-2200

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith. Any such communication will be deemed to have been given (i) when delivered on a Business Day, if personally delivered or sent by facsimile or other electronic means (subject to confirmation of such delivery), on such Business Day, (ii) when delivered other than on a Business Day, if personally delivered or sent by facsimile or other electronic means (subject to confirmation of such delivery), on the first Business Day after dispatch, (iii) on the Business Day after dispatch, if sent by nationally-recognized overnight courier, and (iv) on the third Business Day following the date of mailing, if sent by mail. It is understood and agreed that this Section 8.8 is not intended to govern the day-to-day business communications necessary between the Parties in performing their duties, in due course, under the terms of this Master Agreement.

8.9 Expenses. Each Party will pay all costs and expenses that it incurs with respect to the negotiation, execution, delivery and performance of this Master Agreement and the other Transaction Documents.

8.10 Titles and Subtitles. The titles of the sections and subsections of this Master Agreement are for convenience of reference only and are not to be considered in construing this Master Agreement.

8.11 Counterparts. This Master Agreement may be executed in any number of counterparts, each of which will be an original, but all of which together will constitute one instrument. This Master Agreement and any signed agreement or instrument entered into in connection with this Master Agreement, and any amendments hereto or thereto, to the extent signed and delivered by means of a facsimile machine or other electronic means, shall be treated in all manner and respects as an original agreement or instrument and shall be considered to have the same binding legal effect as if it were the original signed version thereof delivered in person. At the request of any Party hereto or to any such agreement or instrument, each other Party hereto or thereto shall re-execute original forms thereof and deliver them to all other parties. No Party hereto or to any such agreement or instrument shall raise the use of a facsimile machine or other electronic means to deliver a signature or the fact that any signature or agreement or instrument was transmitted or communicated through the use of a facsimile machine or other electronic means as a defense to the formation of a contract and each such Party forever waives any such defense.

8.12 Construction. The Parties acknowledge and agree that they have been represented by counsel during the negotiation, preparation and execution of this Master Agreement and, therefore, waive the application of any Law or rule of construction providing that ambiguities in an agreement or other document shall be construed against the Party drafting such agreement or document. Where specific language is used to clarify by example a general statement contained herein, such specific language shall not be deemed to modify, limit or restrict in any manner the construction of the general statement to which it relates. When the context so requires the word "or" when used herein shall mean "and/or." All pronouns contained herein, and any variations thereof, will be deemed to refer to the masculine, feminine or neutral, singular or plural, as to the identity of the Parties hereto may require. Other than with respect to Section 2 and the preamble to Section 3.1, the words, "provided to," "delivered" or "made available" or words of similar import when used in this Master Agreement to refer to obligations of Isis and/or Ibis to "provide," "deliver" or "make available" materials to AMI will mean "made available in the online dataroom maintained by Isis at [***] by 12:00 p.m. Pacific time on or before January 23, 2008."

8.13 No Other Compensation.

The Parties hereby agree that the terms of the Investment Documents fully define all consideration, compensation and benefits, monetary or otherwise, to be paid, granted or delivered by Isis or Ibis to AMI or Abbott and by AMI or Abbott to Isis or Ibis in connection with the transactions contemplated herein and therein. Except pursuant to the Permitted Employee Compensation Plan, no Party previously has paid or entered into any other commitment to pay, whether orally or in writing, any employee of any other Party, directly or indirectly, any consideration, compensation or benefits, monetary or otherwise, in connection with the transactions contemplated in the Transaction Documents.

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IN WITNESS WHEREOF, the parties hereto have executed this **STRATEGIC ALLIANCE MASTER AGREEMENT** as of the date set forth in the first paragraph hereof.

ISIS PHARMACEUTICALS, INC.

Signature: /s/ B. Lynne Parshall

Print Name: B. Lynne Parshall

Title: COO & CFO

Address:

IBIS BIOSCIENCES, INC.

Signature: /s/ Michael J Treble

Print Name: Michael J Treble

Title: President

Address:

ABBOTT MOLECULAR INC.

Signature: /s/ Stafford O'Kelly

Print Name: Stafford O'Kelly

Title: President

Address:

SIGNATURE PAGE TO STRATEGIC ALLIANCE MASTER AGREEMENT

LIST OF EXHIBITS

EXECUTION VERSION

EXHIBIT A

INVESTOR RIGHTS AGREEMENT

BY AND AMONG

ISIS PHARMACEUTICALS, INC.,

IBIS BIOSCIENCES, INC.

AND

ABBOTT MOLECULAR INC.

January 30, 2008

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IBIS BIOSCIENCES, INC.

INVESTOR RIGHTS AGREEMENT

THIS INVESTOR RIGHTS AGREEMENT (this "Agreement") is made and entered into as of this 30th day of January, 2008, by and among Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"), Ibis Biosciences, Inc., a Delaware corporation ("Ibis"), and Abbott Molecular Inc., a Delaware corporation ("AMI"). Isis, Ibis and AMI are sometimes referred to herein individually as a "Party," and collectively as the "Parties."

RECITALS

WHEREAS, AMI, Isis and Ibis have formed a strategic alliance pursuant to the Strategic Alliance Master Agreement, of even date herewith (the "Master Agreement");

WHEREAS, pursuant to the Master Agreement, AMI is purchasing the Shares and may, in its sole discretion, subscribe for and purchase the Additional Shares pursuant to the Call Option Agreement and the Stock Subscription Agreement;

WHEREAS, the execution and delivery of this Agreement by Isis and Ibis is a material inducement to AMI to enter into the Master Agreement and the other Transaction Documents; and

WHEREAS, in connection with the consummation of the Financing, the Parties desire to enter into this Agreement in order to grant registration, information, protective and other rights to AMI as set forth below.

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, and covenants set forth herein and in the Master Agreement and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1. General.

1.1 Definitions.

Capitalized terms used and not otherwise defined herein have the meanings ascribed to such terms in the Master Agreement. In addition to terms defined elsewhere herein and in the Master Agreement, the following terms when used in this Agreement have the following meanings:

(a) "Additional Shares" means 114,250 shares of Common Stock that may be acquired by AMI from Ibis in AMI's sole discretion prior to 5:00 p.m. (Pacific Time) on the Cut-Off Date pursuant to the Call Option Agreement and the Stock Subscription Agreement, as may be held from time to time by AMI and its permitted assigns, which, together with the Shares, will represent approximately 18.6% of the issued and outstanding Common Stock at the time of such issuance.

(b) "Change of Control" means, with respect to any Person, the occurrence of (i) any consolidation or merger of such Person with or into any other Person, or any other corporate reorganization or transaction (including the acquisition of Capital Stock of such Person (or any rights to acquire, or securities convertible into or exchangeable for, any such Capital Stock)), whether or not such Person is a party thereto, in which the stockholders or equity-holders of such Person or other Persons controlling such Person immediately prior to such consolidation, merger, reorganization or transaction, own Capital Stock either (A) representing directly, or indirectly through one or more entities, less than fifty percent (50%) of the economic interests in or voting power of such Person or other surviving entity immediately after such consolidation, merger, reorganization or transaction or (B) that does not directly, or indirectly through one or more entities, have the power to elect a majority of the entire board of directors or equivalent governing body of such Person or other surviving entity immediately after such consolidation, merger, reorganization or transaction or (ii) a sale, lease, license or other disposition of all or a material portion of the assets of such Person.

(c) "Equivalent Shares" means, at any date of determination, (i) as to any outstanding shares of Common Stock, such number of shares of Common Stock and (ii) as to any outstanding options, warrants or other convertible securities which are directly or indirectly convertible into or exchangeable or exercisable for shares of Common Stock, the maximum number of shares of Common Stock for which or into which such options, warrants or other convertible securities may at the time be exercised, converted or exchanged (or which shall become exercisable, convertible or exchangeable on or prior to, or by reason of, the transaction or circumstance in connection with which the number of Equivalent Shares is to be determined).

(d) "Exchange Act" means the Securities Exchange Act of 1934, as amended.

(e) "Holder" means any Person owning of record Registrable Securities.

(f) "Initial Offering" means Ibis' first firm commitment underwritten Offering of its Common Stock registered under the Act.

(g) "Make Whole Event" means (i) a Change of Control of Ibis, (ii) any liquidation, dissolution, share exchange, business combination or recapitalization of Ibis, or (iii) a Change of Control of Isis pursuant to which such transferee, successor or acquiring Person does not assume Isis' obligations under the Investment Documents; *provided* that a Change of Control arising in connection with a Transfer by Isis pursuant to and in compliance with Section 3.6 or a Change of Control arising in connection with an Issuance in compliance with Section 3.7 shall *not* be a Make Whole Event.

(h) "Offering" means a public offering of Ibis' Common Stock registered under the Act.

(i) "Register," "registered," and "registration" refer to a registration effected by preparing and filing a registration statement in compliance with the Act, and the declaration or ordering of effectiveness of such registration statement or document.

(j) "Registrable Securities" means the Shares. Notwithstanding the foregoing, Registrable Securities shall not include any securities (i) sold by a Person to the public either pursuant to a registration statement or Rule 144 or (ii) sold in a private transaction in which the transferee does not become a party to this Agreement.

(k) "Registration Expenses" means all expenses incurred by Ibis in complying with Sections 2.2 or 2.3 of this Agreement, including, without limitation, all underwriter expenses (not including underwriter discounts), registration and filing fees and printing expenses, legal fees, Blue Sky fees and expenses and the expense of any special audits incident to or required by any such registration (but excluding the compensation of regular employees of Ibis which shall be paid in any event by Ibis).

(l) "Shares" means (i) 114,251 shares of Common Stock issued to AMI pursuant to the Master Agreement, representing approximately 10.25% of the issued and outstanding Common Stock (whether held by AMI or any transferee of AMI in accordance with the terms of this Agreement), (ii) the Additional Shares, if AMI exercises the Subscription Right and acquires the Additional Shares pursuant to the Call Option Agreement and the Stock Subscription Agreement and (iii) any Capital Stock issued as (or issuable upon the conversion or exercise of any Capital Stock which is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, such above-described securities.

(m) "Special Registration Statement" means (i) a registration statement relating to any employee benefit plan or equity incentive plan for directors, officers and/or consultants, (ii) with respect to any corporate reorganization or transaction under Rule 145 of the Act, any registration statements related to the issuance or resale of securities issued in such a transaction, or (iii) a registration related to the distribution by Isis to Isis' stockholders of shares of Common Stock held by Isis.

(n) "Subsequent Closing" means, if AMI exercises the Subscription Right and acquires the Additional Shares, the consummation of such acquisition.

(o) "Transfer" means any sale, pledge, hypothecation, assignment, Encumbrance or other transfer or disposition, whether directly, indirectly, voluntarily, involuntarily, by operation of Law, pursuant to judicial process or otherwise, and, when the context so requires, the act of doing any of the foregoing.

1.2 Table of Defined Terms. Section references for definitions of defined terms defined in the body of this Agreement rather than in this Section 1.

Term	Section
"Abbott Holders"	Section 2.1(d)
"Act"	Section 2.1(e)
"Agreement"	Preamble
"AMI"	Preamble
"Demand Registration Notice"	Section 2.2(a)
"Holder Violation"	Section 2.7(b)

"Holder Indemnified Party"	Section 2.7(a)
"Ibis"	Preamble
"Ibis Indemnified Party"	Section 2.7(b)
"Initiating Stockholder"	Section 2.3(b)
"Isis"	Preamble
"Issuance	Section 3.7
"Issuer"	Section 3.7
"Make Whole Payment"	Section 4.1
"Master Agreement"	Recitals
"Participating Buyer"	Section 3.7(b)
"Participating Seller"	Section 3.6(b)
"Participation Notice"	Section 3.7(a)
"Participation Offerees"	Section 3.7(a)
"Participation Portion"	Section 3.7(a)(i)
"Prospective Buyer"	Section 3.6(a)(i)

"Prospective Subscriber"	Section 3.7(a)(i)
"Participating Holder Majority"	Section 2.5(a)
"Party" and "Parties"	Preamble
"Rule 144"	Section 2.1(b)(iii)
"Sale Notice"	Section 2.1(d)(i)
"Subject Securities"	Section 3.7
"Suspension Period"	Section 2.5(a)
"Tag Along Holder"	Section 3.6(a)
"Tag Along Notice"	Section 3.6(a)
"Tag Along Offer"	Section 3.6(b)
"Tag Along Sellers"	Section 3.6(b)
"Third Party Demand Registration"	Section 2.3(b)
"Violation"	Section 2.7(a)

2. Restrictions on Transfer; Registration Rights.

2.1 Restrictions on Transfer.

(a) Before the Call Option Expiration Date AMI cannot Transfer all or any portion of the Shares or Registrable Securities.

(b) After the Call Option Expiration Date, AMI and its transferees cannot Transfer all or any portion of the Shares or Registrable Securities unless and until:

(i) there is then in effect a registration statement under the Act covering such proposed disposition and such disposition is made in accordance with such registration statement;

(ii) if reasonably requested by Ibis, in connection with any Transfer not covered by Section 2.1(b)(i) or Section 2.1(b)(iii) hereof, Ibis has received an

opinion of counsel, reasonably satisfactory to Ibis, that such disposition shall not require registration of such Shares or Registrable Securities under the Act; or

(iii) such Shares or Registrable Securities may be transferred pursuant to Rule 144, as promulgated under the Act ("Rule 144").

(c) Notwithstanding the provisions of Section 2.1(a) and Section 2.1(b) above and Section 2.1(d) below, no restrictions contained in such Sections shall apply to a Transfer by AMI to any of its Affiliates or to Transfers between Affiliates of AMI; *provided* that in such case the transferee agrees in writing to be bound by the terms of this Agreement; and *provided further* that any such Transfer to an Affiliate of AMI is for no fewer than [***] Shares per Transfer.

(d) AMI and its Affiliate transferees, if any (collectively, the "Abbott Holders"), hereby grant to Isis a right of first refusal with respect to the Shares held by such Abbott Holders on the following terms:

(i) If, after the Call Option Expiration Date, an Abbott Holder proposes to Transfer any of the Shares, then such Abbott Holder shall promptly give written notice (the "Sale Notice") to Ibis and to Isis at least [***] prior to the closing of such Transfer. The Sale Notice shall describe in reasonable detail the proposed Transfer including, without limitation, the number of Shares to be transferred, the nature of such Transfer, the consideration to be paid, and the name and address of each prospective purchaser or transferee.

(ii) Following receipt of any Sale Notice from an Abbott Holder, Isis shall have the right, within [***] after receipt of the Sale Notice, to elect in a written notice to such Abbott Holder, with a copy to Ibis, to purchase the Shares described in the Sale Notice from such Abbott Holder for cash in an amount equal to the consideration to be paid in the proposed Transfer. Upon such election, Ibis shall have [***] from the date of the Sale Notice to consummate its acquisition of the Shares described in the Sale Notice. The exercise or non-exercise of the rights of Isis hereunder to participate in one or more Transfers by Abbott Holders shall not adversely affect Isis' right to participate in subsequent Transfers of Shares by Abbott Holders.

(iii) To the extent Isis does not within such [***] period elect to purchase the Shares described in the Sale Notice or does not consummate such purchase within such [***] period, (A) the Abbott Holder submitting the Sale Notice may, not later than [***] following delivery to Isis of the Sale Notice, enter into an agreement providing for the closing of the Transfer of such Shares within [***] of the date of such agreement, or as soon thereafter as reasonably practicable, on terms and conditions that when taken as a whole are not materially less favorable to such Abbott Holder than those described in the Sale Notice and (B) Ibis and Isis shall reasonably cooperate in good faith with such Abbott Holder to consummate such Transfer. Any proposed Transfer on terms and conditions materially less favorable to such Abbott Holder than those described in the Sale Notice, as well as any subsequent proposed Transfer of any of the Shares by such Abbott Holder, shall again be subject to the rights of Isis and shall require compliance by such Abbott Holder with the procedures described in this Section 2.1(d). Notwithstanding anything to the contrary contained herein, the provisions of this Section 2.1(d)

shall not apply to any subsequent Transfers by any prospective purchaser or transferee of Shares that are not Abbott Holders following the consummation of the Transfer contemplated by the Sale Notice.

(iv) The provisions of this Section 2.1(d) shall terminate following the closing of an Initial Offering.

(e) Each certificate representing Registrable Securities shall be stamped or otherwise imprinted with legends substantially similar to the following (in addition to any legend required under applicable state securities laws):

> THE SECURITIES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933 (THE "***ACT***") AND MAY NOT BE OFFERED, SOLD OR OTHERWISE TRANSFERRED, ASSIGNED, PLEDGED OR HYPOTHECATED UNLESS AND UNTIL REGISTERED UNDER THE ACT OR ENTITLED TO AN AVAILABLE EXEMPTION THEREFROM.
>
> THE SALE, PLEDGE, HYPOTHECATION OR TRANSFER OF THE SECURITIES REPRESENTED BY THIS CERTIFICATE IS SUBJECT TO THE TERMS AND CONDITIONS OF A CERTAIN INVESTOR RIGHTS AGREEMENT BY AND BETWEEN THE STOCKHOLDER AND THE COMPANY. COPIES OF SUCH AGREEMENT MAY BE OBTAINED UPON WRITTEN REQUEST TO THE SECRETARY OF THE COMPANY.

(f) Ibis shall be obligated to reissue promptly unlegended certificates at the request of AMI or any of its transferees if Ibis has completed an Offering and Ibis has been furnished with an opinion of counsel (which counsel may be counsel to Ibis) reasonably acceptable to Ibis to the effect that the securities proposed to be disposed of may lawfully be so disposed of without registration, qualification and legend; *provided that* the *second* legend listed above shall be removed only from (i) Registrable Securities the Holders of which are not subject to any restrictions hereunder or (ii) Shares that have been Transferred to a transferee who is not an Abbott Affiliate and does not become a party to this agreement.

2.2 Right to Cause an Offering.

(a) After the Call Option Expiration Date, AMI, by providing written notice (a "Demand Registration Notice") to Ibis, may demand that Ibis file a registration statement under the Act to effect an Offering of all of the Registrable Securities. Upon receipt of a Demand Registration Notice, Ibis shall use its reasonable best efforts to effect, as expeditiously as reasonably possible, such Offering, including the registration under the Act of all Registrable Securities, on terms reasonably requested by AMI. Subject to the consent of Ibis, which shall not be unreasonably withheld, conditioned or delayed, AMI shall have the right to select the underwriter or underwriters in connection with any Offering made pursuant to a Demand Registration Notice.

(b) Notwithstanding the foregoing, Ibis shall not be required to effect a registration pursuant to this Section 2.2:

(i) prior to the Call Option Expiration Date;

(ii) during the period beginning on the date of filing of, and ending on the date that is the earlier of (A) [***] following the date of the filing of or (B) [***] following the effective date of, the registration statement pertaining to an Offering initiated by Ibis (or such longer period as may be determined pursuant to Section 2.8 hereof); provided that Ibis uses its reasonable best efforts to cause such registration statement to become effective;

(iii) if within [***] of receipt of a Demand Registration Notice, Ibis furnishes to AMI a certificate signed by the Chairman of the Board of Directors of Ibis stating that in the good faith judgment of the Board of Directors of Ibis, it would be seriously detrimental to Ibis and its stockholders for such registration statement to be effected at such time, Ibis shall have the right to defer such filing for a period of not more than [***] after receipt of such Demand Registration Notice; provided that such right to delay a request may be exercised by Ibis not more than once in any [***] period; or

(iv) if such registration is for less than [***] percent ([***]%) of the Shares.

(c) All Holders proposing to distribute their Registrable Securities through an Offering pursuant to this Section 2.2 shall enter into an underwriting agreement in customary form and reasonably satisfactory to each of Ibis and AMI.

2.3 Piggyback Registrations.

(a) Ibis shall notify all Holders of Registrable Securities in writing at least twenty (20) days prior to the filing of any registration statement under the Act for purposes of an Offering (including, but not limited to, Offerings initiated at the request of a third party, but excluding Special Registration Statements), and shall afford each such Holder an opportunity to include in such registration statement all or part of such Registrable Securities held by such Holder. Each Holder desiring to include in any such registration statement all or any part of the Registrable Securities held by it shall, within [***] after the above-described notice from Ibis, so notify Ibis in writing. Such notice shall state the intended method of disposition of the Registrable Securities by such Holder. If a Holder decides not to include all of its Registrable Securities in any registration statement thereafter filed by Ibis, such Holder shall nevertheless continue to have the right to include any Registrable Securities in any subsequent registration statement or registration statements as may be filed by Ibis with respect to Offerings of its securities, all upon the terms and conditions set forth herein.

(b) If the registration statement of which Ibis gives notice under this Section 2.3 is for an underwritten Offering, Ibis shall so advise the Holders of Registrable Securities. In such event, the right of any such Holder to include Registrable Securities in a

registration pursuant to this Section 2.3 shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their Registrable Securities through such underwriting shall enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting by Ibis. Notwithstanding any other provision of this Agreement, if the underwriter determines in good faith that marketing factors require a limitation of the number of shares to be underwritten, the number of shares that may be included in the underwriting shall be allocated in accordance with the following terms. If the Offering is for the account of Ibis or Isis and cannot accommodate all of the Registrable Securities requested by Abbott Holders to be registered, each of the other selling stockholders shall be cut back (including Isis and selling stockholders who are transferees of AMI but not Abbott Holders), pro rata, based on the

number of shares for which registration was requested by each such selling stockholder, to the maximum extent possible before the Registrable Securities requested by Abbott Holders to be registered are cut back. If an Offering is made pursuant to a demand made by a stockholder (the "Initiating Stockholder") that is not AMI or a stockholder acting for the account of Ibis or Isis (a "Third Party Demand Registration") and cannot accommodate all of the Registrable Securities requested by Abbott Holders to be registered, each of the other selling stockholders (other than the Initiating Stockholder) shall be cut back (including selling stockholders who are transferees of AMI but not Abbott Holders), pro rata, based on the number of shares for which registration was requested by each such selling stockholder, to the maximum extent possible before the Registrable Securities requested by Abbott Holders to be registered are cut back. If any Holder disapproves of the terms of any such underwriting, such Holder may elect to withdraw therefrom by written notice to Ibis and the underwriter, delivered at least [***] prior to the effective date of the registration statement. Any Registrable Securities excluded or withdrawn from such underwriting shall be excluded and withdrawn from the registration. For any Holder which is a partnership, limited liability company or corporation, the partners, retired partners, members, retired members and stockholders of such Holder, or the estates and family members of any such partners, retired partners, members, retired members and stockholders and any trusts for the benefit of any of the foregoing persons shall be deemed to be a single "selling stockholder." For purposes of the preceding sentence, all Abbott Holders will be treated as a single "selling stockholder."

(c) Ibis shall have the right to terminate or withdraw any registration initiated by it under this Section 2.3 whether or not any Holder has elected to include securities in such registration. The Registration Expenses of such withdrawn registration shall be borne by Ibis in accordance with Section 2.4 hereof.

2.4 Expenses of Registration. Except as specifically provided herein, all Registration Expenses incurred in connection with any registration, qualification or compliance pursuant to Section 2.2 or Section 2.3 herein shall be borne by Ibis. All underwriter discounts incurred in connection with any registrations hereunder shall be borne by the holders of the securities so registered. Holders participating in a registration proceeding shall be required to pay for reasonable Registration Expenses for any registration proceeding begun pursuant to Section 2.2, the request of which has been subsequently withdrawn by AMI unless (a) the withdrawal is based upon material adverse information concerning Ibis of which AMI was not aware at the time of such request or (b) AMI agrees to deem such registration to have been effected as of the date of such withdrawal for purposes of determining whether Ibis shall be

obligated pursuant to Section 2.2 to undertake any subsequent registration, in which event such right shall be forfeited by AMI and all other Holders. If the Holders are required to pay the Registration Expenses, such expenses shall be borne by the stockholders (including Holders and any other stockholders of Ibis that would have participated in such registration proceeding) *pro* rata based on the number of shares for which registration was requested by each such Holder or other stockholder.

2.5 Obligations of Ibis. Whenever required to effect the registration of any Registrable Securities, Ibis shall, as expeditiously as reasonably possible:

(a) prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its reasonable best efforts to cause such registration statement to become effective, and, upon the request of Holders of at least 50% of the Registrable Securities so registered (a "Participating Holder Majority"), keep such registration statement effective for up to [***] [***] or, if earlier, until the Holder or Holders have completed the distribution related thereto; *provided* that at any time, upon written notice to all Holders whose Registrable Securities were so registered, for a period not to exceed [***] thereafter (the "Suspension Period"), Ibis may delay the filing or effectiveness of any registration statement or suspend the use or effectiveness of any registration statement (and such Holders hereby agree not to offer or sell any Registrable Securities pursuant to such registration statement during the Suspension Period) if Ibis reasonably believes that there is or may be in existence material nonpublic information or events involving Ibis, the failure of which to be disclosed in the prospectus included in the registration statement could result in a Violation (as defined below). In the event that Ibis exercises its right to delay or suspend the filing or effectiveness of a registration hereunder, the applicable time period during which the registration statement is to remain effective shall be extended by a period of time equal to the duration of the Suspension Period. Ibis may extend the Suspension Period for an additional consecutive [***] with the consent of a Participating Holder Majority, which consent shall not be unreasonably withheld. If so directed by Ibis, Holders shall (i) not offer to sell any Registrable Securities pursuant to the registration statement during any Suspension Period; and (ii) use their reasonable best efforts to deliver to Ibis (at Ibis' expense) all copies, other than permanent file copies then in its possession, of the prospectus relating to such Registrable Securities current at the time of receipt of such notice. Notwithstanding the foregoing, Ibis shall not be required to file, cause to become effective or maintain the effectiveness of any registration statement other than (A) a registration statement pursuant to Section 2.2 or (B) a registration statement on Form S-3 that contemplates a distribution of securities on a delayed or continuous basis pursuant to Rule 415 under the Act.

(b) Prepare and file with the SEC such amendments and supplements to such registration statement and the prospectus used in connection with such registration statement as may be necessary to comply with the provisions of the Act with respect to the disposition of all securities covered by such registration statement for the period set forth in Section 2.5(a) above.

(c) Furnish to the Holders such number of copies of a prospectus, including a preliminary prospectus, in conformity with the requirements of the Act, and such other documents as they may reasonably request in order to facilitate the disposition of Registrable Securities owned by them.

(d) Use its reasonable best efforts to register and qualify the securities covered by such registration statement under such other securities or Blue Sky laws of such jurisdictions as may be reasonably requested by any Holder covered by such registration statement; *provided* that Ibis shall not be required in connection therewith or as a condition thereto to qualify to do business or to file a general consent to service of process in any such states or jurisdictions.

(e) In the event of any underwritten Offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the managing underwriter(s) of such Offering. Each Holder participating in such underwriting shall also enter into and perform its obligations under such an agreement.

(f) Notify each Holder covered by such registration statement at any time when a prospectus relating thereto is required to be delivered under the Act of the happening of any event as a result of which the prospectus included in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing. Ibis shall use its reasonable best efforts to amend or supplement such prospectus in order to cause such prospectus not to include any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing.

(g) Use its reasonable best efforts to furnish, on the date that such Registrable Securities are delivered to the underwriters for sale, if such securities are being sold through underwriters, (i) an opinion, dated as of such date, of the counsel representing Ibis for the purposes of such registration, in form and substance as is customarily given to underwriters in an underwritten public offering, addressed to the underwriters, if any, and (ii) a comfort letter, dated as of such date (including any requested updates thereto), from the independent certified public accountants of Ibis, in form and substance as is customarily given by independent certified public accountants to underwriters in an underwritten public offering addressed to the underwriters.

2.6 Delay of Registration; Furnishing Information.

(a) No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any such registration as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

(b) It shall be a condition precedent to the obligations of Ibis to take any action pursuant to Section 2.2, Section 2.3 or Section 2.5 that the selling Holders shall furnish to Ibis such information regarding themselves, the Registrable Securities held by them and the intended method of disposition of such securities as shall be reasonably required to effect the registration of their Registrable Securities.

2.7 Indemnification. In the event any Registrable Securities are included in a registration statement under Sections 2.2 or 2.3, whichever is applicable:

(a) To the extent permitted by law, Ibis and, as long as Isis holds [***] or more of the Equivalent Shares outstanding immediately following the completion of the Offering contemplated by such Registration Statement, Isis shall, jointly and severally, indemnify and hold harmless each Holder, the partners, members, officers, directors, stockholders, employees, representatives, agents and Affiliates of each Holder, any underwriter (as defined in the Act) for such Holder and each person, if any, who controls such Holder or underwriter within the meaning of the Act or the Exchange Act (each a "Holder Indemnified Party"), against any Losses to which it may become subject under the Act, the Exchange Act or other federal or state law, insofar as such Losses arise out of or are based upon any of the following statements, omissions or violations (collectively a "Violation") by Ibis: (i) any untrue statement or alleged untrue statement of a material fact contained in such registration statement or incorporated by reference therein, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto, (ii) the omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading, or (iii) any violation or alleged violation by Ibis of the Act, the Exchange Act, any state securities law or any rule or regulation promulgated under the Act, the Exchange Act or any Blue Sky law in connection with the Offering covered by such registration statement; *provided* that the indemnity obligations contained in this Section 2.7(a) shall not apply to amounts paid in settlement of any Loss if such settlement is effected without the consent of Ibis, which consent shall not be unreasonably withheld, conditioned or delayed, nor shall Ibis or Isis be liable in any such case for any such Loss to the extent that it arises out of or is based upon a Violation which occurs in reliance upon and in conformity with written information furnished expressly for use in connection with such registration by such Holder Indemnified Party (or with respect to the Abbott Holders, any Abbott Holder).

(b) To the extent permitted by law, each Holder shall indemnify and hold harmless Ibis, the partners, members, officers, directors, stockholders, employees, representatives, agents and Affiliates of Ibis, any underwriter (as defined in the Act) for Ibis and each person, if any, who controls Ibis or such underwriter within the meaning of the Act or the Exchange Act (each an "Ibis Indemnified Party") against any Losses to which it may become subject under the Act, the Exchange Act or other federal or state law, insofar as such Losses arise out of or are based upon any of the following: (i) any untrue statement or alleged untrue statement of a material fact contained in such registration statement or incorporated reference therein, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto, (ii) the omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading, or (iii) any violation or alleged violation by Ibis of the Act (collectively, a "Holder Violation"), in each case to the extent (and only to the extent) that such Holder Violation occurs in reliance upon and in conformity with written information furnished by such Holder under an instrument duly executed by such Holder and stated to be specifically for use in connection with such registration (it being understood and agreed that solely for purposes of and notwithstanding the foregoing, the Abbott Holders shall jointly and severally indemnify and hold harmless the Ibis Indemnified Parties against Losses arising out of or based upon any Holder Violation by any Abbott Holder); *provided* that the indemnity obligations contained in this Section 2.7(b) shall not apply to amounts paid in settlement of any such Loss, if such settlement is effected without the consent of such Holder, which consent shall not be unreasonably withheld, conditioned or delayed; *provided further*, that in no event shall any indemnity under this Section 2.7 exceed the

net proceeds from the Offering received by such Holder (it being understood and agreed that solely with respect to this provision, all of the Abbott Holders will be considered one Holder for purposes of calculating the net proceeds from the Offering to any particular Abbott Holder).

(c) Promptly after receipt by an indemnified party under this Section 2.7 of notice of the commencement of any action (including any governmental action), such indemnified party shall, if a claim in respect thereof is to be made against any indemnifying party under this Section 2.7, deliver to the indemnifying party a written notice of the commencement thereof and the indemnifying party shall have the right to participate in, and, to the extent the indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume the defense thereof with counsel mutually satisfactory to the parties; *provided* that an indemnified party shall have the right to retain its own counsel, with the fees and expenses thereof to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would, in the view of such indemnified party, be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such proceeding. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of any liability to the indemnified party under this Section 2.7 to the extent, and only to the extent, prejudicial to its

ability to defend such action, but the omission so to deliver written notice to the indemnifying party shall not relieve it of any liability that it may have to any indemnified party otherwise than under this Section 2.7.

(d) If the indemnification provided for in this Section 2.7 is held by a court of competent jurisdiction to be unavailable to an indemnified party with respect to any Loss referred to herein, the indemnifying party, in lieu of indemnifying such indemnified party thereunder, shall to the extent permitted by applicable law contribute to the amount paid or payable by such indemnified party as a result of such loss, claim, damage or liability in such proportion as is appropriate to reflect the relative fault of the indemnifying party on the one hand and of the indemnified party on the other in connection with the Violation(s) or Holder Violation(s) that resulted in such Loss as well as any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by a court of law by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission to state a material fact relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission; *provided*, that in no event shall any contribution by a Holder, hereunder exceed the net proceeds from the Offering received by such Holder.

(e) The obligations of Ibis, Isis and each Holder under this Section 2.7 shall survive completion of any Offering of Registrable Securities in a registration statement and, with respect to liability arising from an Offering to which this Section 2.7 would apply that is covered by a registration filed before termination of this Agreement, such termination. No indemnifying party, in the defense of any such claim or litigation, shall, except with the consent of each indemnified party, consent to entry of any judgment or enter into any settlement which (i) does not include as an unconditional term thereof the giving by the claimant or plaintiff to each indemnified party of a release from all liability in respect to such claim or litigation or (ii) contains an admission of liability or guilt or imposes any liability or obligation on the indemnified party.

2.8 "Market Stand-Off" Agreement. Each Holder hereby agrees that it shall not sell, Transfer, make any short sale of, grant any option for the purchase of, or enter into any hedging or similar transaction with the same economic effect as a sale, any Capital Stock of Ibis held by such Holder (other than those included in the registration) during (a) the [***] period following the effective date of the Initial Offering (or such longer period, not to exceed [***] after the expiration of the [***] period, as the underwriters or Ibis shall request in order to facilitate compliance with NASD Rule 2711), and (b) the [***] period following the effective date of a registration statement of Ibis filed under the Act (or such longer period, not to exceed [***] after the expiration of [***], as the underwriters or Ibis shall request in order to facilitate compliance with NASD Rule 2711); *provided* that, with respect to (a) and (b) above, all stockholders holding [***]% or more of Ibis' then outstanding Capital Stock (other than to the extent such stockholders are participating in such registration) and all officers and directors of Ibis are bound by and have entered into similar agreements. Ibis may impose stop-transfer instructions with respect to the shares of Capital Stock subject to the foregoing restriction until the end of the stand-off period. The obligations described in this Section 2.8 shall not apply to a registration relating solely to employee benefit plans on Form S-1 or Form S-8 or similar forms that may be promulgated in the future, or a registration relating solely to a transaction on Form S-4 or similar forms that may be promulgated in the future.

2.9 Agreement to Furnish Information. Each Holder hereby agrees to execute and deliver such other agreements as may be reasonably requested by Ibis or the underwriter that are consistent with such Holder's obligations under this Agreement or that are necessary to give further effect thereto. In addition, if requested by Ibis or the representative of the underwriters of Common Stock (or other securities) of Ibis, such Holder shall provide, within [***] of such request, such information as may be required by Ibis or such representative in connection with the completion of any Offering of Ibis' securities pursuant to a registration statement filed under the Act. The obligations described in Section 2.8 and this Section 2.9 shall not apply to a Special Registration Statement. The underwriters of Ibis' stock are intended third party beneficiaries of Section 2.8 and this Section 2.9 only and will have the right, power and authority to enforce such provisions as though they were a party hereto.

2.10 Rule 144 Reporting. With a view to making available to the Holders the benefits of certain rules and regulations of the SEC which may permit the sale of the Registrable Securities to the public without registration, Ibis agrees to use its reasonable best efforts to:

(a) Make and keep public information available, as those terms are understood and defined in Rule 144 or any similar or analogous rule promulgated under the Act, at all times after the effective date of the first registration filed by Ibis for an Offering of its securities to the general public;

(b) File with the SEC, in a timely manner, all reports and other documents required of Ibis under the Exchange Act; and

(c) So long as a Holder owns any Registrable Securities, furnish to such Holder forthwith upon request: a written statement by Ibis as to its compliance with the reporting requirements of Rule 144, and of the Exchange Act (at any time after it has become subject to such reporting requirements); a copy of the most recent annual or quarterly report of Ibis filed with the Commission; and such other reports and documents as a Holder may reasonably request in connection with availing itself of any rule or regulation of the SEC allowing it to sell any such securities without registration.

2.11 Termination of Registration Rights. The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to Section 2.2 or Section 2.3 hereof shall terminate upon the earlier of: (a) the date [***] following an Initial Offering; or (b) following the Initial Offering, such time as all Registrable Securities issuable or issued upon conversion of the Shares held by and issuable to such Holder (and its Affiliates) may be sold pursuant to Rule 144 during any [***] period.

3. Covenants of the Isis Parties.

3.1 Use of Proceeds. The proceeds from the Financing shall be used exclusively to fund the operations of the Ibis business, including, without limitation, research and development related to the Assay Kit Milestone and the Value Accretion Milestones (as each such term is defined in the Call Option Agreement). Furthermore, no portion of the proceeds from the Financing may be transferred to or used for the benefit of (except as an indirect benefit via Isis' ownership of the Remaining Shares) Isis except as expressly (a) required by the Corporate Services Agreement, (b) Section 3 of the Contribution Agreement, or (c) contemplated by Section 7.10 of the Acquisition Agreement.

3.2 Basic Financial Information and Reporting.

(a) Ibis shall maintain true books and records of account in which full and correct entries shall be made of all its business transactions pursuant to a system of accounting established and administered in accordance with GAAP (except as noted therein or as disclosed to the recipients thereof), and shall set aside on its books all such proper accruals and reserves as shall be required under GAAP.

(b) For as long as any Abbott Holder holds any Shares, subject to AMI's confidentiality obligations pursuant to Sections 5.1, 5.2 and 5.3 of the Master Agreement, as soon as practicable after the end of each fiscal year of Ibis, and in any event within one hundred twenty (120) days thereafter, Ibis shall furnish to AMI a balance sheet of Ibis, as at the end of such fiscal year, and a statement of results from operations and a statement of cash flows of Ibis, for such year, all prepared in accordance with GAAP (except as noted therein or as disclosed to the recipients thereof). In addition, Ibis shall include a summary report comparing the results from operations to the budget approved by Ibis' Board of Directors. Such financial statements shall be signed by the senior financial officer of Ibis or be prepared by a nationally recognized accounting firm.

(c) For as long as Abbott Holders hold at least [***]% of the Shares, Ibis shall furnish to AMI: (i) beginning with the 2009 fiscal year, at least thirty (30) days prior to

the beginning of each fiscal year, an annual budget (and a statement of the assumptions embodied therein) for such fiscal year that has been approved by Ibis' Board of Directors (and as soon as available, any subsequent written revisions thereto); and (ii) as soon as practicable after the end of each calendar quarter, and in any event within forty five (45) days thereafter, a balance sheet of Ibis as of the end of each such quarter, and a statement of income and a statement of cash flows of Ibis for such quarter and for the current fiscal year to date, including a comparison to plan figures for such period, prepared in accordance with GAAP (except as noted thereon or as disclosed to the recipients thereof), with the exception that no notes need be attached to such statements and year-end audit adjustments may not have been made. Such financial statements shall be signed by the senior financial officer of Ibis or be prepared by a nationally recognized accounting firm. Ibis shall deliver the 2008 annual budget and related statement of assumptions to AMI on the date hereof.

(d) After the Call Period and for as long as Abbott Holders hold at least [***]% of the Shares, AMI shall have the right to visit and inspect any of the properties of Ibis, and to discuss the affairs, finances and accounts of Ibis with Ibis' officers and Board of Directors, and to review such information as is reasonably requested all at such reasonable times and as often as may be reasonably requested; *provided* that Ibis shall not be obligated under this Section 3.2(d) with respect to information which the Ibis Board of Directors determines in good faith is highly confidential or attorney-client privileged and should not, therefore, be disclosed.

3.3 Sale of Shares. Ibis and Isis shall take all reasonable actions requested by any Abbott Holder in connection with any Transfer by such Abbott Holder of the Shares to any proposed transferee after the Call Option Expiration Date, including, without limitation, cooperating in good faith with any due diligence efforts undertaken by any proposed transferee.

3.4 Board Observer. For as long as Abbott Holders hold at least [***]% of the Shares, AMI shall be entitled to have a representative of AMI attend all meetings of the Ibis Board of Directors (which, in any event Ibis and Isis shall cause to occur not less than once per calendar quarter upon no less than 5 Business Days prior written notice to AMI) in a nonvoting observer capacity and, in this respect, Ibis shall give such representative copies of all notices, minutes, consents, and other material that it provides to its directors not less than 3 Business Days prior to each such meeting, *provided* that Ibis may withhold information or materials or exclude AMI's representative from meetings as reasonably necessary to preserve the attorney-client privilege or in the event of a conflict of interest. AMI agrees, and any representative of AMI shall agree, that information provided to AMI's representative shall be Confidential Information of Ibis subject to Sections 5.1, 5.2 and 5.3 of the Master Agreement.

3.5 Restrictions on Transfer. Prior to the Call Option Expiration Date, Isis cannot Transfer any of the Capital Stock of Ibis held by it, *except* if (a) such Transfer is in connection with a Change of Control of Isis, (b) such Transfer involves all of the Capital Stock of Ibis that is owned by Isis and (c) the surviving or acquiring entity assumes all of Isis' obligations under the Investment Documents.

3.6 Tag Along. Following the Call Option Expiration Date and for as long as any Shares remain outstanding, if Isis proposes to Transfer any Capital Stock of Ibis for consideration (other than a Transfer in connection with a Change of Control of Isis that involves

all of the Capital Stock of Ibis that is owned by Isis and an assignment is made by Isis in accordance with Section 5.2 hereof), then:

(a) Isis shall deliver a written notice (the "Tag Along Notice") to each holder of Shares (each, a "Tag Along Holder") at least twenty (20) Business Days prior to such proposed Transfer. The Tag Along Notice shall include:

(i) The principal terms of the proposed Transfer, including (A) with respect to each class of Capital Stock to be transferred, the purchase price for such Capital Stock, (B) with respect to each class of Capital Stock to be transferred, the total number of shares of such Capital Stock Isis proposes to Transfer, (C) the name and address of the prospective transferee (the "Prospective Buyer") and (D) the draft sale agreement with the Prospective Buyer, if available (and if not available, promptly after it becomes available); and

(ii) With respect to each class of Capital Stock to be transferred, an invitation to each Tag Along Holder to make an offer to include in the proposed Transfer to the Prospective Buyer a number of Shares held by such Tag Along Holder on the same terms and conditions as Isis is proposing to Transfer such Capital Stock.

(b) Within ten (10) Business Days after the delivery of the Tag Along Notice, each Tag Along Holder desiring to make an offer to include Shares in the proposed Transfer (each a "Participating Seller" and, together with Isis, collectively, the "Tag Along Sellers") shall furnish a written notice (the "Tag Along Offer") to Isis offering to include, with respect to each class of Capital Stock to be transferred, a number of Shares which such Participating Seller desires to have included in the proposed Transfer. With respect to each class of Capital Stock to be transferred, each Tag Along Holder who does not accept Isis' invitation to make an offer to include any Shares in the proposed Transfer shall be deemed to have waived all of its rights with respect to such Transfer, and the Tag Along Sellers shall thereafter be free to Transfer to the Prospective Buyer, at a per share price no greater than the per

share price set forth in the Tag Along Notice and on other principal terms which are not materially more favorable to the Tag Along Sellers than those set forth in the Tag Along Notice, without any further obligation to such non-accepting Tag Along Holder.

(c) Isis shall attempt to obtain the inclusion in the proposed Transfer of the entire number of Shares which each of the Tag Along Sellers requested to have included in the Transfer (as evidenced in the case of Isis by the Tag Along Notice and in the case of each Participating Seller by such Participating Seller's Tag Along Offer). In the event Isis shall be unable to obtain the inclusion of such entire number of Shares in the proposed Transfer, the number of shares of Ibis Common Stock to be sold in such proposed Transfer shall be allocated to each Tag Along Seller in proportion to, as nearly as practicable, the proportion the Shares held by such Tag Along Seller bears to the total number of shares of Ibis Common Stock held by all the Tag Along Sellers. To the extent a Tag Along Seller elects to include less than its full allocation of Shares in the proposed Transfer, the portion not included in the proposed Transfer shall be allocated to the Tag Along Sellers (who are not able to include in the proposed Transfer all of the Shares identified in their Tag Along Offer) in the same manner as set forth in this Section 3.6(c).

(d) If the Tag-Along Sellers have not completed the proposed Transfer by the end of the 180th day following the delivery of the Tag Along Notice, each Participating Seller shall be released from its obligations under its Tag Along Offer, the Tag Along Notice shall be null and void, and it shall be necessary for a separate Tag Along Notice to be furnished, and the terms and provisions of this Section 3.6 separately complied with, in order to consummate such proposed Transfer pursuant to this Section 3.6, unless the failure to complete such proposed Transfer resulted from any failure by any Participating Seller to comply with the terms of this Section 3.6.

3.7 Right of Participation. Prior to the Call Option Expiration Date Ibis shall not, and shall not permit any of its Subsidiaries (Ibis and any such Subsidiary, an "Issuer") to, issue or sell any Capital Stock or enter into any agreements providing for the issuance (contingent or otherwise) of, any of its Capital Stock (each an "Issuance" of "Subject Securities"). After the Call Option Expiration Date and for as long as any Shares remain outstanding, no Issuer shall initiate or commence any Issuance, except in compliance with the provisions of this Section 3.7.

(a) Offer. Not fewer than ten (10) Business Days prior to the consummation of an Issuance, a notice (the "Participation Notice") shall be furnished by the Issuer to each holder of Shares (the "Participation Offerees"). The Participation Notice shall include:

(i) The principal terms of the proposed Issuance, including (A) the amount and kind of Subject Securities to be included in the Issuance, (B) the number of Equivalent Shares represented by such Subject Securities (if applicable), (C) the percentage of the total number of Equivalent Shares outstanding as of immediately prior to giving effect to such Issuance that are held by such Participation Offeree (the "Participation Portion"), (D) the maximum and minimum price per unit of the Subject Securities, (E) the name and address of the Person to whom the Subject Securities shall be issued (the "Prospective Subscriber") and (F) the sale agreement with the Prospective Subscriber, if available (and if not available, promptly after it becomes available); and

(ii) An offer by the Issuer to issue, at the option of each Participation Offeree, to such Participation Offeree such portion of the Subject Securities to be included in the Issuance as may be requested by such Participation Offeree (not to exceed the Participation Portion of the total amount of Subject Securities to be included in the Issuance), on the same terms and conditions, with respect to each unit of Subject Securities issued to the Participation Offerees, as each of the Prospective Subscribers shall be issued units of Subject Securities.

(b) Each Participation Offeree desiring to accept the offer contained in the Participation Notice shall send a written commitment to the Issuer within ten (10) Business Days after the delivery of the Participation Notice specifying the amount of Subject Securities (not in any event to exceed the Participation Portion of the total amount of Subject Securities to be included in the Issuance) which such Participation Offeree desires to be issued (each a "Participating Buyer"). Each Participation Offeree who has not so accepted such offer shall be deemed to have waived all of his rights with respect to the Issuance, and the Issuer shall

thereafter be free to issue Subject Securities in the Issuance to the Prospective Subscriber and any Participating Buyers, at a price not less than the minimum price set forth in the Participation Notice and on other principal terms not materially more favorable to the Prospective Subscriber than those set forth in the Participation Notice, without any further obligation to such non-accepting Participation Offerees. If, prior to consummation, the terms of such proposed Issuance shall change with the result that the price shall be less than the minimum price set forth in the Participation Notice or the other principal terms, when taken as a whole, shall be materially more favorable to the Prospective Subscriber than those set forth in the Participation Notice, it shall be necessary for a separate Participation Notice to be furnished, and the terms and provisions of this Section 3.7 shall be separately complied with, in order to consummate such Issuance pursuant to this Section 3.7.

(c) Time Limitation. If at the end of the 180th day following the date of delivery of the Participation Notice the Issuer has not completed the Issuance, each Participating Buyer shall be released from its obligations under the written commitment, the Participation Notice shall be null and void, and it shall be necessary for a separate Participation Notice to be furnished, and the terms and provisions of this Section 3.7 shall be separately complied with, in order to consummate such Issuance pursuant to this Section 3.7.

(d) Excluded Transactions. The provisions of this Section 3.7 shall not apply to Issuances by any Issuer as follows:

(i) after the Call Option Expiration Date any Issuance of Subject Securities upon the exercise or conversion of any Equivalent Shares issued in compliance with the provisions of this Section 3.7,;

(ii) after the Call Option Expiration Date any Issuance of Subject Securities to officers, employees, directors or consultants of an Issuer in connection with such Person's employment, consulting arrangements or directorship with an Issuer;

(iii) any Issuance of Subject Securities in connection with bona fide, third party strategic commercial transactions as approved by the Ibis Board of Directors, unless such transaction would result in a Change of Control of Ibis where the holders of the Shares would receive

less than the full Make Whole Payment under Section 4.1;

(iv) after the Call Option Expiration Date any Issuance of Subject Securities, pursuant to an Initial Offering where the payment contemplated in Section 4.3 is made;

(v) the Issuance of Subject Securities to AMI in connection with the Financing Closing or the Subsequent Closing; or

(vi) after the Call Option Expiration Date any Issuance of Subject Securities in connection with any stock split, stock dividend, stock combination or stock reclassification.

3.8 Termination.

The provisions of subsections (b)-(d) of Section 3.2, and Sections 3.3 through 3.5, shall terminate following the closing of an Initial Offering and the provisions of Section 3.6 and Section 3.7 shall terminate following the earlier of (i) a Change of Control of Ibis and (ii) the closing of an Initial Offering.

4. Make Whole Provision.

4.1 **Make Whole Payment.** Upon any Make Whole Event, before any distribution or payment shall be made to the holders of any Capital Stock other than holders of Shares with respect to the Shares, holders of Shares shall be entitled to be paid, pro rata according to each such holder's ownership of Shares, out of the proceeds of such Make Whole Event legally available for distribution or payment an aggregate amount equal to the sum of (a) $20,000,000, plus interest thereon at an annual rate of 3% calculated from the date of the Financing Closing on the basis of a 360-day year and (b) if AMI exercises the Subscription Right and acquires the Additional Shares, $20,000,000, plus interest thereon at an annual rate of 3% calculated from the date of the Subsequent Closing on the basis of a 360-day year (the "Make Whole Payment") until the date of such distribution or payment. If, upon any such Make Whole Event, the proceeds of such Make Whole Event are insufficient to make payment in full to all holders of Shares, then all such proceeds shall be paid or distributed to holders of Shares, pro rata according to each such holder's ownership of Shares, without any payment or distribution to any other holders of Capital Stock. If the consideration to be received in such Make Whole Event is securities or property other than cash, such property's value shall be deemed its fair market value as determined in good faith by Ibis' Board of Directors on the date such determination is made.

4.2 Remaining Proceeds. After distribution or payment of the Make Whole Payment, the remaining proceeds of such Make Whole Event legally available for distribution, if any, shall (a) next be distributed ratably to Isis (or any other holders of Common Stock (other than the Shares) after the Call Option Expiration Date) up to an amount per share of Common Stock equal to the amount per Share paid to holders of Shares with respect to the Make Whole Payment and (b) then distributed ratably to all holders of Common Stock (including holders of Shares).

4.3 Initial Offering Termination.

The provisions of this Section 4 shall terminate following the closing of an Initial Offering if, in connection with the closing of such Initial Offering, each Holder receives its pro rata share of an aggregate amount equal to the *interest* payable on each of [***]at an annual rate of [***]calculated from the date of the [***]on the basis of a [***]day year[***], at an annual rate of [***]% calculated from the date of [***]on the basis of a [***]-day year, in each case until the closing of such Initial Offering, payable, at Ibis' election either in cash or in Common Stock based on the price per share of such Initial Offering. If Ibis issues the Holders additional shares of Common Stock under this Section 4.3, such shares will be considered Shares under this Agreement.

4.4 Post Call Period Financing.

In the event that, after the Call Option Expiration Date, Ibis, in compliance with Section 3.7, issues any Capital Stock, then any liquidation preference or other similar preferential distribution rights embodied in the terms of such Capital Stock shall be subordinate to the Holders' right to receive the Make Whole Payment upon a Make Whole Event pursuant to this Section 4. Subject to the foregoing, to the extent reasonably necessary to facilitate such Issuance, the Parties will cooperate in good faith to amend or replace this Section 4 and/or amend Ibis' Certificate of Incorporation.

5. Miscellaneous.

5.1 Governing Law; Alternative Dispute Resolution. This Agreement shall be governed by and construed in accordance with the laws of the State of Delaware without regard to principles of conflicts of law. The Parties agree that any dispute arising from or relating to this Agreement shall be exclusively resolved by the Alternative Dispute Resolution provisions set forth in Exhibit D to the Master Agreement, the result of which shall be binding upon the Parties.

5.2 Assignment. Except as expressly permitted herein, no Party hereto may assign this Agreement or its rights and obligations hereunder without the prior written consent of the other Parties; *provided* that any Abbott Holder may assign its rights and obligations hereunder in connection with its Transfer of Shares in accordance with the terms of this Agreement if (a) within [***] after such Transfer, such Abbott Holder furnishes to Ibis written notice of the name and address of such transferee and (b) such transferee agrees in writing to be bound by the terms of this Agreement; *provided further* that Isis may assign its rights and obligations in connection with a Change of Control of Isis if such Transfer involves all of the Capital Stock of Ibis that is owned by Isis and the surviving or acquiring entity assumes all of Isis' obligations under the Investment Documents. Except as otherwise expressly provided herein, the provisions hereof shall inure to the benefit of, and be binding upon and be enforceable by the Parties and their respective successors, assigns, heirs, executors and administrators.

5.3 No Third Party Beneficiaries. Except as expressly provided in Section 2.9, this Agreement shall not confer any rights or remedies upon any Person other than the parties hereto and their respective successors and permitted transferees and assigns.

5.4 Severability. In the event that any provision of this Agreement, or the application thereof, becomes or is declared by a court of competent jurisdiction to be illegal, void or unenforceable, the remainder of this Agreement shall continue in full force and effect and the application of such provision to other Persons or circumstances shall be interpreted so as reasonably to effect the intent of the Parties hereto. The Parties further agree to replace such void or unenforceable provision of this Agreement with a valid and enforceable provision that shall achieve, to the extent possible, the economic, business and other purposes of such void or unenforceable provision.

5.5 Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one

instrument. This Agreement and any signed agreement or instrument entered into in connection with this Agreement, and any amendments hereto or thereto, to the extent signed and delivered by means of a facsimile machine or other electronic means, shall be treated in all manner and respects as an original agreement or instrument and shall be considered to have the same binding legal effect as if it were the original signed version thereof delivered in person. At the request of any party hereto or to any such agreement or instrument, each other party hereto or thereto shall re-execute original forms thereof and deliver them to all other parties. No party hereto or to any such agreement or instrument shall raise the use of a facsimile machine or other electronic means to deliver a signature or the fact that any signature or agreement or instrument was transmitted or communicated through the use of a facsimile machine or other electronic means as a defense to the formation of a contract and each such party forever waives any such defense.

5.6 Amendment and Waiver. This Agreement may be amended or modified, and the rights and obligations of the Parties under this Agreement may be waived, only upon the written consent of each Party.

5.7 Termination. This Agreement shall terminate and be of no further force or effect upon a Make Whole Event pursuant to which the Make Whole Payment with respect to all the Shares has been indefeasibly made.

5.8 Notices. All notices or other communication that are permitted or required under this Agreement shall be made pursuant to the terms of the Master Agreement.

5.9 Construction.

The Parties acknowledge and agree that they have been represented by counsel during the negotiation, preparation and execution of this Agreement and, therefore, waive the application of any Law or rule of construction providing that ambiguities in an agreement or other document shall be construed against the Party drafting such agreement or document. Where specific language is used to clarify by example a general statement contained herein, such specific language shall not be deemed to modify, limit or restrict in any manner the construction of the general statement to which it relates. When the context so requires, the word “or” when used herein shall mean “and/or.” All pronouns contained herein, and any variations thereof, shall be deemed to refer to the masculine, feminine or neutral, singular or plural, as to the identity of the Parties hereto may require.

5.10 Expenses. Each Party shall pay all costs and expenses that it incurs with respect to the negotiation, execution, delivery and performance of this Agreement.

5.11 Entire Agreement. This Agreement constitutes the full and entire understanding and agreement between the Parties with regard to the subjects hereof and no party shall be liable for or bound to any other in any manner by any oral or written representations, warranties, covenants and agreements except as specifically set forth herein.

5.12 Titles and Subtitles. The titles of the sections and subsections of this Agreement are for convenience of reference only and are not to be considered in construing this Agreement.

5.13 Delays or Omissions. It is agreed that no delay or omission to exercise any right, power or remedy accruing to any Party, upon any breach, default or noncompliance by another Party hereunder or under Ibis’ Certificate of Incorporation, shall impair any such right, power or remedy, nor shall it be construed to be a waiver of any such breach, default or noncompliance, or any acquiescence therein, or of or in any similar breach, default or noncompliance thereafter occurring. It is further agreed that any waiver, permit, consent or approval of any kind or character on any Party’s part of any breach, default or noncompliance hereunder or under Ibis’ Certificate of Incorporation or any waiver on such Party’s part of any provisions or conditions of this Agreement or Ibis’ Certificate of Incorporation must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this Agreement, Ibis’ Certificate of Incorporation, bylaw, or otherwise afforded to any Party, shall be cumulative and not alternative.

[THIS SPACE INTENTIONALLY LEFT BLANK**]**

IN WITNESS WHEREOF, the parties hereto have executed this **INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

ISIS PHARMACEUTICALS, INC.

Signature: _____

Print Name: _____

Title: _____

Address: _____

_____

IBIS BIOSCIENCES, INC.

Signature: _____

Print Name: _____

Title: _____

Address: _____

_____

ABBOTT MOLECULAR INC.

Signature: _____

Print Name: _____

Title: _____

Address: _____

_____

SIGNATURE PAGE FOR INVESTOR RIGHTS AGREEMENT

EXHIBIT B

[CALL OPTION AGREEMENT FILED SEPARATELY AS EXHIBIT 10.5 TO REGISTRANT'S QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED MARCH 31, 2008]

EXHIBIT C

TERMS OF PERMITTED EMPLOYEE COMPENSATION PLAN

AMI and Isis will mutually agree on the [***] package payable by [***]. The money available for such package, in the aggregate, will be [***] of which shall be [***] the Acquisition Closing. Any funds left in [***] would be released to [***].

EXHIBIT D

To begin the ADR process, a Party first must send written notice of the dispute to the other Party for attempted resolution by good faith negotiations between their respective presidents (or their designees) of the affected subsidiaries, divisions, or business units within twenty-eight (28) days after such notice is received (all references to "days" in this ADR provision are to calendar days). If the matter has not been resolved within twenty-eight (28) days after the notice of dispute, or if the parties fail to meet within such twenty-eight (28) days, either Party may initiate an ADR proceeding as provided herein. The parties shall have the right to be represented by counsel in such a proceeding.

To begin an ADR proceeding, a Party shall provide written notice to the other Party of the issues to be resolved by ADR. Within fourteen (14) days after its receipt of such notice, the other Party may, by written notice to the Party initiating the ADR, add additional issues to be resolved within the same ADR.

Within twenty-one (21) days following the initiation of the ADR proceeding, the Parties shall select a mutually acceptable independent, impartial and conflicts-free neutral to preside in the resolution of any disputes in this ADR proceeding. If the Parties are unable to agree on a mutually acceptable neutral within such period, each Party will select one independent, impartial and conflicts-free neutral and those two neutrals will select a third independent, impartial and conflicts-free neutral within ten (10) days thereafter. None of the neutrals selected may be current or former employees, officers or directors of either Party, its Subsidiaries or Affiliates or a current consultant or independent contractor of either Party or its Affiliates.

No earlier than twenty-eight (28) days or later than fifty-six (56) days after selection, the neutral(s) shall hold a hearing to resolve each of the issues identified by the Parties. The ADR proceeding shall take place at a location agreed upon by the Parties. If the Parties cannot agree, the neutral(s) shall designate a location other than the principal place of business of either Party or any of their Affiliates.

At least seven (7) days prior to the hearing, each Party shall submit the following to the other Party and the neutral(s):

a copy of all exhibits on which such Party intends to rely in any oral or written presentation to the neutral;

a list of any witnesses such Party intends to call at the hearing, and a short summary of the anticipated testimony of each witness;

a proposed ruling on each issue to be resolved, together with a request for a specific damage award or other remedy for each issue. The proposed rulings and remedies shall not contain any recitation of the facts or any legal arguments and shall not exceed one (1) page per issue. The Parties agree that neither side shall seek as part of its remedy any punitive damages.

a brief in support of such Party's proposed rulings and remedies, provided that the brief shall not exceed twenty (20) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding

Except as expressly set forth in subparagraphs 4(a) - 4(d), no discovery shall be required or permitted by any means, including depositions, interrogatories, requests for admissions, or production of documents.

The hearing shall be conducted on two (2) consecutive days and shall be governed by the following rules:

Each Party shall be entitled to five (5) hours of hearing time to present its case. The neutral shall determine whether each Party has had the five (5) hours to which it is entitled.

Each Party shall be entitled, but not required, to make an opening statement, to present regular and rebuttal testimony, documents or other evidence, to cross-examine witnesses, and to make a closing argument. Cross-examination of witnesses shall occur immediately after their direct testimony, and cross-examination time shall be charged against the Party conducting the cross-examination.

The Party initiating the ADR shall begin the hearing and, if it chooses to make an opening statement, shall address not only issues it raised but also any issues raised by the responding Party. The responding Party, if it chooses to make an opening statement, also shall address all issues raised in the ADR. Thereafter, the presentation of regular and rebuttal testimony and documents, other evidence, and closing arguments shall proceed in the same sequence.

Except when testifying, witnesses shall be excluded from the hearing until closing arguments.

Settlement negotiations, including any statements made therein, shall not be admissible under any circumstances. Affidavits prepared for purposes of the ADR hearing also shall not be admissible. As to all other matters, the neutral(s) shall have sole discretion regarding the admissibility of any evidence.

Within seven (7) days following completion of the hearing, each Party may submit to the other Party and the neutral(s) a post-hearing brief in support of its proposed rulings and remedies, provided that such brief shall not contain or discuss any new evidence and shall not exceed ten (10) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

The neutral(s) shall rule on each disputed issue within fourteen (14) days following completion of the hearing. Such ruling shall adopt in its entirety the proposed ruling and remedy of one of the Parties on each disputed issue but may adopt one Party's proposed rulings and remedies on some issues and the other Party's proposed rulings and remedies on other issues. T he neutral(s) shall not issue any written opinion or otherwise explain the basis of the ruling.

The neutral(s) shall be paid a reasonable fee plus expenses. These fees and expenses, along with the reasonable legal fees and expenses of the prevailing Party (including all expert witness fees and expenses), the fees and expenses of a court reporter, and any expenses for a hearing room, shall be paid as follows:

If the neutral(s) rule(s) in favor of one Party on all disputed issues in the ADR, the losing Party shall pay 100% of such fees and expenses.

If the neutral(s) rule(s) in favor of one Party on some issues and the other Party on other issues, the neutral(s) shall issue with the rulings a written determination as to how such fees and expenses shall be allocated between the Parties. The neutral(s) shall allocate fees and expenses in a way that bears a reasonable relationship to the outcome of the ADR, with the Party prevailing on more issues, or on issues of greater value or gravity, recovering a relatively larger share of its legal fees and expenses.

The rulings of the neutral(s) and the allocation of fees and expenses shall be binding, non-reviewable, and non-appealable, and may be entered as a final judgment in any court having jurisdiction.

Except as provided in paragraph 9 or as required by law, the existence of the dispute, any settlement negotiations, the ADR hearing, any submissions (including exhibits, testimony, proposed rulings, and briefs), and the rulings shall be deemed Confidential Information. The neutral(s) shall have the authority

to impose sanctions for unauthorized disclosure of Confidential Information.

All ADR hearings shall be conducted in the English language.

EXHIBIT E

PRESS RELEASE

Isis Announces Equity Investment in Ibis Biosciences Subsidiary by Abbott; Option Acquired to Purchase Remaining Ibis Equity

- Conference call webcast Thursday, January 31, 2008, 8:30 a.m. EST at www.isispharm.com

CARLSBAD, Calif., Jan 31, 2008 /PRNewswire-FirstCall via COMTEX News Network/ — Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that Abbott is investing up to $40 million in Ibis Biosciences, Inc., an Isis subsidiary. The investment will allow Ibis to further develop the Ibis T5000(TM) Biosensor System, which offers a unique solution for rapid identification and characterization of infectious agents that can identify virtually all bacteria, viruses and fungi, and can provide information about drug resistance, virulence and strain type of these pathogens within a few hours.

Under the terms of the agreement, Abbott will initially acquire approximately 10.25 percent of the equity in Ibis for $20 million. Abbott will have the right to invest an additional $20 million before July 31, 2008 for a total of 18.6 percent of Ibis equity. Abbott will also receive an exclusive option to purchase the remaining equity in Ibis for an additional $175 to $195 million through June 30, 2009 plus an earn out tied to achievement of certain cumulative sales. The option exercise price can increase to up to $190 to $210 million with Ibis' successful completion of pre-negotiated milestones.

"This investment by Abbott reflects the significant value we have built through our Ibis business," said Michael Treble, President of Ibis. "We have been successful in commercializing our products for various government, epidemiology and clinical research applications, and we are excited about expanding our markets to hospital-based infections and, eventually, to diagnostics. We believe that this investment will allow us to accelerate the evolution of the Ibis technology to address our biggest market opportunity: clinical diagnostics."

"Ibis is a tangible example of the value of the innovation taking place at Isis and of our strategy," said B. Lynne Parshall, COO and CFO of Isis. "The investment by Abbott provides Ibis the funding to take the key next steps in enhancing its value. Because of the transaction structure, even if the option is exercised, Isis shareholders will continue to benefit from Ibis' success through the earn out provision. As a result we believe this is a very attractive transaction for Isis shareholders."

Conference Call

At 8:30 a.m. Eastern Standard Time today, January 31, 2008, Isis will conduct a live webcast conference call to discuss this transaction. Interested parties may access the webcast at http://www.isispharm.com or listen to the call by dialing 877-440-5796. A webcast replay will be available for a limited time at the same address.

ABOUT IBIS T5000 BIOSENSOR SYSTEM AND IBIS BIOSCIENCES, INC.

Ibis Biosciences, Inc., a majority-owned subsidiary of Isis Pharmaceuticals, has developed and is commercializing the Ibis T5000(TM) Biosensor System for rapid identification and characterization of infectious agents. The Ibis T5000 is currently intended for research use only and not for use in diagnostic procedures. It is capable of identifying virtually all bacteria, viruses and fungi, and can provide information about drug resistance, virulence and strain type of these pathogens. Commercial applications for the Ibis T5000 Biosensor System include epidemiologic surveillance, monitoring of pandemic diseases, identification of emerging or previously unknown pathogens, forensic characterization of human samples, identification of sources of hospital-associated infections, and, in the future, human infectious disease diagnostics. Ibis develops, manufactures and markets Ibis T5000 instruments and assay kits, including through its partner, Bruker Daltonics, a subsidiary of Bruker BioSciences Corporation. Additional information about Ibis can be found by selecting the Ibis link from Isis' homepage at http://www.isispharm.com.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 18 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Ibis Biosciences, Inc., Isis' majority-owned subsidiary, is developing and commercializing the Ibis T5000(TM) Biosensor System, a revolutionary system to identify infectious organisms. Isis is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development and commercialization of microRNA therapeutics. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,500 issued patents worldwide. Additional information about Isis is available at http://www.isispharm.com.

This release includes forward-looking statements regarding Abbott's investment in Isis' subsidiary, Ibis, and the development and commercialization of the Ibis T5000 Biosensor System and Ibis' technology. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' goals or projections. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, in developing and commercializing systems to identify infectious organisms that are effective and commercially attractive, and in the endeavor of building a business around such products. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently

known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2006, and its quarterly report

on Form 10-Q for the quarter ended September 30, 2007, which are on file with the SEC. Copies of this and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R §§ 200.80(b)4, AND 240.24b-2

EXECUTION VERSION

CALL OPTION AGREEMENT

BY AND AMONG

ISIS PHARMACEUTICALS, INC.,

IBIS BIOSCIENCES, INC.

AND

ABBOTT MOLECULAR INC.

January 30, 2008

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CALL OPTION AGREEMENT

THIS CALL OPTION AGREEMENT (this "Agreement") is made and entered into as of this 30th day of January 2008, by and among Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"), Ibis Biosciences, Inc., a Delaware corporation ("Ibis"), and Abbott Molecular Inc., a Delaware corporation ("AMI"). Isis, Ibis and AMI are sometimes referred to herein individually as a "Party," and collectively as the "Parties."

RECITALS

WHEREAS, on the date hereof, the Parties have entered into a Strategic Alliance Master Agreement (the "Master Agreement") and certain other Investment Documents, pursuant to which, among other things, AMI has acquired the Shares from Ibis;

WHEREAS, in connection with the transactions contemplated by the Investment Documents, Isis has agreed to grant an option to AMI and AMI has agreed to acquire from Isis an option for AMI to acquire all of the Capital Stock (other than the Shares (and the Additional Shares if AMI elects to acquire the Additional Shares pursuant to the Stock Subscription Agreement)) of Ibis (the "Optioned Stock") from Isis on the terms set forth in this Agreement and the Acquisition Agreement;

WHEREAS, in connection with the transactions contemplated by the Investment Documents, Ibis has agreed to grant a subscription right to AMI and AMI has agreed to acquire from Ibis a subscription right to subscribe for and acquire the Additional Shares from Ibis on the terms set forth in this Agreement and the Stock Subscription Agreement; and

WHEREAS, the execution and delivery of this Agreement by Isis and Ibis is a material inducement for AMI to enter into the Master Agreement and to acquire the Shares.

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, and covenants hereinafter set forth and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

ARTICLE I

DEFINITIONS

Capitalized terms used but not defined herein have the meanings ascribed to such terms in the Master Agreement. In addition to the terms defined elsewhere herein and in the Master Agreement, the following terms when used in this Agreement have the following meanings:

"Acquisition Agreement" means the form of Stock Purchase Agreement attached hereto as Exhibit A.

"Call Option Expiration Date" means 5:00 p.m. (Pacific Time) on the date the Call Option expires pursuant to the terms hereof, which, subject to Section 3.1, Section 3.2, Section 3.3 and Section 3.4, shall be December 31, 2008.

"Call Period" means the period of time commencing on the date hereof and ending on the Call Option Expiration Date.

"Cut-Off Date" means, subject to Section 3.2, 5:00 p.m. (Pacific Time) on July 31, 2008.

"Stock Subscription Agreement" means the form of Stock Subscription Agreement attached hereto as Exhibit B.

ARTICLE II

GRANT OF CALL OPTION; SUBSCRIPTION RIGHTS

Section 2.1 Grant of Option. Subject to the terms set forth in this Agreement, Isis hereby grants to AMI, and AMI hereby acquires from Isis, an exclusive option, in AMI's sole discretion (the "Call Option"), to purchase the Optioned Stock on the terms set forth in this Agreement and in the Acquisition Agreement.

Section 2.2 Subscription Right. Subject to the terms set forth in this Agreement, Ibis hereby grants to AMI, and AMI hereby acquires from Ibis the exclusive right, in AMI's sole discretion (the "Subscription Right"), to subscribe for and purchase the Additional Shares on the terms set forth in this Agreement and in the Stock Subscription Agreement for an aggregate purchase price of $20,000,000.

Section 2.3 Purchase Price. The "Transaction Value" for the Optioned Stock shall be equal to (a) either (i) One Hundred Seventy Five Million and No/100 Dollars ($175,000,000.00) if AMI has exercised the Subscription Right and acquired the Additional Shares or (ii) One Hundred Ninety Five

Million and No/100 Dollars ($195,000,000.00) if AMI has not exercised the Subscription Right (the "Base Purchase Price") plus (b) the Milestone Adjustments (as defined below), if any.

Section 2.4 Milestone Adjustments. If AMI, in good faith, determines that the [***] Milestone (as set forth in Exhibit C hereto) has been reached prior to AMI's delivery to Isis of the Option Notice or Isis' delivery to AMI of the Purchase Offer Notice (as defined below), as the case may be, then:

(a) if AMI, in good faith, also determines that the [***] Milestone (as set forth in Exhibit C hereto) has been reached as of the date of the Option Notice or the Purchase Offer Notice, as the case may be, then the Transaction Value shall be increased by [***] (the "[***] Milestone Adjustment");

(b) if AMI, in good faith, also determines that the [***] Milestone (as set forth in Exhibit C hereto) has been reached as of the date of the Option Notice or the Purchase Offer

Notice, as the case may be, then the Transaction Value shall be increased by [***] (the "[***] Milestone Adjustment"); and

(c) if AMI, in good faith, also determines that the [***] Milestone (as set forth in Exhibit C hereto) has been reached as of the date of the Option Notice or the Purchase Offer Notice, as the case may be, then the Transaction Value shall be increased by [***] (the "[***] Milestone Adjustment" and, together with the [***] Milestone Adjustment and the [***] Milestone Adjustment, the "Milestone Adjustments").

The Milestone Adjustments shall not, under any circumstances, exceed Fifteen Million and No/100 Dollars ($15,000,000.00) in the aggregate, and the Transaction Value shall not, under any circumstances, exceed, in the aggregate (1) One Hundred Ninety Million and No/100 Dollars ($190,000,000.00) if AMI has exercised the Subscription Right and acquired the Additional Shares or (2) Two Hundred Ten Million and No/100 Dollars ($210,000,000.00) if AMI has not exercised the Subscription Right.

ARTICLE III

EXERCISE OF OPTION

Section 3.1 Exercise of Call Option.

(a) AMI, in its sole discretion at any time prior to the Call Option Expiration Date, may exercise the Call Option by executing and delivering to Isis the Option Notice attached hereto as Exhibit D (the "Option Notice"). If AMI exercises the Call Option in accordance with this Section 3.1, then in the Option Notice AMI shall instruct Isis and Ibis to execute and deliver to AMI, promptly upon receipt of the Option Notice, the Acquisition Agreement and the Disclosure Schedules thereto (which shall be the most recent Disclosure Schedules delivered by Isis pursuant to Section 3.6(a), unless otherwise agreed to by the Parties in writing).

(b) If the Disclosure Schedules attached to the Acquisition Agreement executed and delivered by Isis and Ibis pursuant to Section 3.1(a) are the most recent Disclosure Schedules delivered by Isis pursuant to Section 3.6(a), then the Call Option shall automatically expire if AMI, in its sole discretion, does not execute and deliver the Acquisition Agreement to Isis within five (5) Business Days after AMI's receipt of the executed Acquisition Agreement.

(c) If the Disclosure Schedules attached to the Acquisition Agreement executed and delivered by Isis and Ibis pursuant to Section 3.1(a) are not the most recent Disclosure Schedules delivered by Isis pursuant to Section 3.6(a), then the Call Option shall automatically expire if AMI, in its sole discretion, does not execute and deliver the Acquisition Agreement to Isis on or prior to the later of (i) the date that is one month after AMI's receipt of the executed Acquisition Agreement and (ii) the Call Option Expiration Date (which, in this instance, subject to Section 3.3 and Section 3.4, is December 31, 2008).

Section 3.2 Exercise of Subscription Right.

(a) AMI, in its sole discretion at any time prior to the Cut-Off Date, may exercise the Subscription Right by providing written notice to Isis. If AMI exercises the Subscription Right in accordance with this Section 3.2, then, promptly upon receipt of notice from AMI, Ibis and Isis shall execute and deliver to AMI the Stock Subscription Agreement and the Disclosure Schedules thereto (which shall be the most recent Disclosure Schedules delivered by Isis pursuant to Section 3.6(a), unless otherwise agreed to by the Parties in writing).

(b) If the Disclosure Schedules attached to the Stock Subscription Agreement executed and delivered by Isis and Ibis pursuant to Section 3.2(a) are the most recent Disclosure Schedules delivered by Isis pursuant to Section 3.6(a), then the Subscription Right and the Call Option shall automatically expire if AMI, in its sole discretion, does not execute and deliver the Stock Subscription Agreement to Isis within five (5) Business Days after AMI's receipt of the executed Stock Subscription Agreement.

(c) If the Disclosure Schedules attached to the Stock Subscription Agreement executed and delivered by Isis and Ibis pursuant to Section 3.2(a), above are not the most recent Disclosure Schedules delivered by Isis pursuant to Section 3.6(a), then the Subscription Right and the Call Option shall automatically expire if AMI, in its sole discretion, does not execute and deliver the Stock Subscription Agreement and acquire the Additional Shares on or prior to August 31, 2008.

(d) Subject to Section 3.2(a), Section 3.2(b) and Section 3.2(c), in the event that Isis or Ibis or any of their respective Representatives receives a Purchase Offer within [***] of the Cut-Off Date, then the Cut-Off Date shall be the Call Acceleration Date.

Section 3.3 Call Option Extension. If the [***] Milestone has not been met on or before [***], then AMI, in its sole discretion and without the payment of any additional consideration, may elect to extend the Call Option Expiration Date to June 30, 2009, by providing written notice to Ibis at any time prior to 11:59 p.m. (Pacific Time) on [***]

Section 3.4 Call Option Acceleration.

(a) If, during the Call Period, Isis or Ibis or any of their respective Representatives receives a Purchase Offer, then Isis shall, within [***] after such receipt, notify AMI in writing of such Purchase Offer, setting forth in such notice (the "Purchase Offer Notice") [***] and indicating therein whether, assuming that the conditions in Section 3.4(b) have been met, it intends to pursue such Purchase Offer.

(b) If (i) the Purchase Offer is from an unaffiliated third party and is unsolicited, bona fide and in writing, (ii) the [***], (iii) AMI has not exercised the Call Option, (iv) the consummation of the Purchase Offer would result in AMI [***] in exchange for the surrender of the Shares and, if AMI has exercised the Subscription Right and acquired the Additional Shares, [***] in exchange for the surrender of the Additional Shares and (v) in such Purchase Offer Notice, Isis indicates that it desires to pursue the Purchase Offer, then the Call Option Expiration Date shall accelerate to the date which is [***] days (the "Call Acceleration Date") from the date on which AMI receives such Purchase Offer Notice.

(c) At any time prior to 5:00 p.m. (Pacific Time) on the Call Acceleration Date, AMI shall have the right, in its sole discretion, to exercise the Call Option for either (i) [***], or (ii) [***]; *provided* that, if AMI, in its sole discretion, elects option (ii) above, the Acquisition Closing shall be consummated [***]. If AMI does not exercise the Call Option prior to 5:00 p.m. (Pacific Time) on the Call Acceleration Date, then the Call Option shall expire.

(d) If Isis or Ibis (as applicable) fails to consummate the transactions contemplated by such Purchase Offer on terms no less favorable to Isis or Ibis (as applicable) than those indicated in the Purchase Offer Notice within [***] days from the date of the Purchase Offer Notice (the "Purchase Offer Termination Date"), then (i) Isis and Ibis shall be prohibited from pursuing the Purchase Offer, (ii) the Call Option shall be reinstated, (iii) the Call Period shall be extended automatically to the date that is the later of (A) [***] days after the Purchase Offer Termination Date and (B) [***] days after the Call Option Expiration Date (giving effect to any extensions thereof, but disregarding any acceleration of such date pursuant to Section 3.4(b)) and (iv) during the Call Period, Isis and Ibis shall not be permitted to entertain any subsequent offers from the third party that submitted such Purchase Offer.

Section 3.5 Effect of Expiration and Termination of Call Option, Subscription Right. After (a) the Call Option Expiration Date (subject to Section 3.4(d)) or (b) if AMI exercises the Call Option, (i) the termination of the Acquisition Agreement in accordance with its terms or (ii) the Acquisition Closing, (A) this Agreement shall terminate automatically and the Call Option and Subscription Right shall be null and void and of no further force or effect without any further action by the Parties and (B) Isis, Ibis and AMI shall have no further rights or obligations under this Agreement. Except as expressly set forth in any Investment Document, the expiration of the Call Period shall not affect the rights and obligations of any of the parties hereto and thereto.

Section 3.6 Call Option Exercise and Subscription Right Exercise Preparation.

(a) AMI may, in connection with its good faith determination whether to exercise in its sole discretion the Subscription Right or the Call Option, request that Isis deliver the Disclosure Schedules to the Stock Subscription Agreement or the Acquisition Agreement, as the case may be, to AMI and, thereafter, Isis shall, as soon as reasonably possible, deliver to AMI the Disclosure Schedules to the Stock Subscription Agreement or the Acquisition Agreement, as the case may be, together with a certification of an authorized signatory of Isis that the representations and warranties set forth in the Stock Subscription Agreement or the Acquisition Agreement, as the case may be, as qualified by the Disclosure Schedules, are true and correct in all respects as of the date of delivery to AMI. In any event, Isis shall deliver the Disclosure Schedules to the Stock Subscription Agreement to AMI no later than June 30, 2008.

(b) Isis and Ibis shall reasonably cooperate with AMI to (i) obtain all necessary waivers, consents and approvals and (ii) effect all necessary registrations, filings and submissions that may be required in connection with the consummation of the transactions contemplated by the Transaction Documents, including, but not limited to, A) filings under the Hart Scott Rodino Antitrust Improvements Act of 1976, as amended and any other submissions requested by the Federal Trade Commission or Department of Justice and (B) such filings,

consents, approvals, orders, registrations and declarations as may be required under the Laws of any foreign country.

ARTICLE IV

MISCELLANEOUS PROVISIONS

Section 4.1 Assignment. No Party hereto may assign this Agreement or its rights and obligations hereunder without the prior written consent of the other Parties; *provided*, that AMI may (i) designate one or more of its Affiliates to exercise the Call Option or Subscription Right hereunder or to receive title to the Optioned Stock or Additional Shares by providing written notice to Ibis at any time prior to the Acquisition Closing or the acquisition of the Additional Shares and (ii) assign its rights and obligations hereunder in connection with a Change of Control of AMI; *provided further* that Isis may assign its rights and obligations in connection with a Change of Control of Isis if such Transfer involves all of the Capital Stock of Ibis that is owned by Isis and the surviving or acquiring entity assumes all of Isis' obligations under the Investment Documents.

Section 4.2 Notices. All notices or other communications that are required or permitted under this Agreement will be in writing and delivered personally with acknowledgement of receipt, sent by facsimile or other electronic means (and promptly confirmed by personal delivery, registered or certified mail or overnight courier as provided herein), sent by nationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, addressed as follows:

If to Ibis, to:

Ibis Biosciences Inc.
1896 Rutherford Road
Carlsbad, California 92008
Attn: President
Facsimile Number: (760) 603-4653

If to Isis, to:

Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, California 92008
Attn: Chief Financial Officer
Facsimile Number: (760) 603-4650

with a copy to:

Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, California 92008
Attn: General Counsel
Facsimile Number: (760) 268-4922

If to AMI, to: Abbott Laboratories
Corporate Transactions and Medical Products Legal Operations
Dept. 322, Bldg. AP6A
100 Abbott Park Road
Abbott Park, Illinois 60064-6010
Attn: Vice President and Associate General Counsel
Facsimile Number: (847) 938-1206

with a copy to: Kirkland & Ellis LLP
200 East Randolph Drive
Chicago, Illinois 60601
Attn:R. Scott Falk, P.C.
Facsimile Number: (312) 861-2200

or to such other address as the Party to whom notice is to be given may have furnished to the other Parties in writing in accordance herewith. Any such communication will be deemed to have been given (i) when delivered on a Business Day, if personally delivered or sent by facsimile or other electronic means (subject to confirmation of such delivery), on such Business Day, (ii) when delivered other than on a Business Day, if personally delivered or sent by facsimile or other electronic means (subject to confirmation of such delivery), on the first Business Day after dispatch, (iii) on the first Business Day after dispatch, if sent by nationally-recognized overnight courier, and (iv) on the third Business Day following the date of mailing, if sent by mail. It is understood and agreed that this Section 4.2 is not intended to govern the day-to-day business communications necessary between the Parties in performing their duties, in due course, under the terms of this Agreement.

Section 4.3 Counterparts. This Agreement may be executed in any number of counterparts, each of which will be an original, but all of which together will constitute one instrument. This Agreement and any signed agreement or instrument entered into in connection with this Agreement, and any amendments hereto or thereto, to the extent signed and delivered by means of a facsimile machine or other electronic means, shall be treated in all manner and respects as an original agreement or instrument and shall be considered to have the same binding legal effect as if it were the original signed version thereof delivered in person. At the request of any Party hereto or to any such agreement or instrument, each other Party hereto or thereto shall re-execute original forms thereof and deliver them to all other Parties. No Party hereto or to any such agreement or instrument shall raise the use of a facsimile machine or other electronic means to deliver a signature or the fact that any signature or agreement or instrument was transmitted or communicated through the use of a facsimile machine or other electronic means as a defense to the formation of a contract and each such Party forever waives any such defense.

Section 4.4 Amendment. This Agreement may be amended or modified, and the rights and obligations of the Parties under this Agreement may be waived, only upon the written consent of each Party.

Section 4.5 Severability. In the event that any provision of this Agreement, or the application thereof, becomes or is declared by a court of competent jurisdiction to be illegal, void or unenforceable, the remainder of this Agreement shall continue in full force and effect and the

application of such provision to other Persons or circumstances shall be interpreted so as reasonably to effect the intent of the Parties hereto. The Parties further agree to replace such void or unenforceable provision of this Agreement with a valid and enforceable provision that will achieve, to the extent possible, the economic, business and other purposes of such void or unenforceable provision.

Section 4.6 Remedies Cumulative. Except as otherwise provided herein, any and all remedies herein expressly conferred upon a Party shall be deemed cumulative with and not exclusive of any other remedy conferred hereby, or by law or equity upon such Party, and the exercise by a Party of any one remedy shall not preclude the exercise of any other remedy.

Section 4.7 Governing Law; Alternative Dispute Resolution. This Agreement shall be governed by and construed in accordance with the laws of the State of Delaware without regard to principles of conflicts of law. The Parties agree that any dispute arising from or relating to this Agreement shall be exclusively resolved by the Alternative Dispute Resolution procedures set forth in Exhibit D to the Master Agreement, the result of which shall be binding upon the Parties.

Section 4.8 Rules of Construction. The Parties acknowledge and agree that they have been represented by counsel during the negotiation, preparation and execution of this Agreement and, therefore, waive the application of any Law or rule of construction providing that ambiguities in an agreement or other document shall be construed against the Party drafting such agreement or document. Where specific language is used to clarify by example a general statement contained herein, such specific language shall not be deemed to modify, limit or restrict in any manner the construction of the general statement to which it relates. When the context so requires the word "or" when used herein shall mean "and/or." All pronouns contained herein, and any variations thereof, will be deemed to refer to the masculine, feminine or neutral, singular or plural, as the identity of the Parties may require.

Section 4.9 Further Assurances. Each of the Parties to the Agreement shall use commercially reasonable efforts to effectuate the transactions contemplated hereby. Each Party hereto, at the reasonable request of another Party hereto, shall execute and deliver such other instruments and do and perform such other acts and things as may be necessary or desirable for effecting completely the consummation of this Agreement and the transactions contemplated hereby.

* * * * *

[Remainder of page intentionally left blank; Signatures on following page]

IN WITNESS WHEREOF, Isis, Ibis and AMI each have caused this Call Option Agreement to be executed and delivered in their names by their respective duly authorized officers or representatives.

ISIS:

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall
Name: B. Lynne Parshall
Title: COO & CFO

IBIS:

IBIS BIOSCIENCES, INC.

By: /s/ Michael J Treble
Name: Michael J Treble
Title: President

AMI:

ABBOTT MOLECULAR INC.

By: /s/ Stafford O'Kelly
Name: Stafford O'Kelly
Title: President

SIGNATURE PAGE TO CALL OPTION AGREEMENT

EXHIBIT A

STOCK PURCHASE AGREEMENT

by and among

IBIS BIOSCIENCES, INC.,

ISIS PHARMACEUTICALS, INC.

and

Dated:

[,]

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STOCK PURCHASE AGREEMENT

THIS STOCK PURCHASE AGREEMENT (this "Agreement") is made and entered into as of this [ ] day of [,], by and among Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"), Ibis Biosciences, Inc., a Delaware corporation and majority owned subsidiary of Isis ("Ibis"), and Abbott Molecular Inc., a Delaware corporation ("AMI") and Affiliate of Abbott Laboratories, an Illinois corporation ("Abbott"). AMI, Ibis and Isis are sometimes referred to herein individually as a "Party" and collectively as the "Parties."

WHEREAS, on January 30, 2008, the Parties entered into the Master Agreement, the Call Option Agreement and the Investor Rights Agreement, pursuant to which, among other things, AMI acquired the Shares and the Call Option for an aggregate purchase price of $20,000,000;

[WHEREAS, on **[ ]**, 2008, the Parties entered into the Stock Subscription Agreement, pursuant to which, among other things, AMI acquired the Additional Shares for an aggregate purchase price of $20,000,000;**]**

WHEREAS, Isis owns 1,000,000 shares of Ibis' Common Stock (the "Remaining Shares");

WHEREAS, on [ ] **[**200], pursuant to the terms of the Call Option Agreement, AMI exercised the Call Option, electing to acquire the Remaining Shares pursuant to the terms hereof; and

WHEREAS, subject to the terms and conditions set forth in this Agreement, Isis desires to sell to AMI and AMI desires to acquire from Isis the Remaining Shares.

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, and covenants hereinafter set forth and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

Section 1. DEFINITIONS. Capitalized terms used and not otherwise defined herein have the meanings ascribed to such terms in this Section 1.

(a) "Abbott Transaction Team" means the individuals listed on Schedule 1(a).

(b) [**"**Additional Shares" means 114,250 shares of Common Stock acquired by AMI pursuant to the Stock Subscription Agreement, as may be held from time to time by AMI and its permitted assigns, which, together with the Shares, represent approximately 18.6% of the issued and outstanding Common Stock.]

(c) "Affiliate" of an entity means any other entity that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such first entity. For purposes of this definition only, "control" (and, with correlative meanings, the terms "controlled by" and "under common control with") means the possession, directly or indirectly, of the power to direct the management or policies of an entity, whether through the ownership of voting securities or by Contract relating to voting rights or corporate governance; *provided*, that (i) with respect to AMI and Abbott, the term "Affiliate" shall specifically exclude [***] and (ii) with respect to Isis, the term "Affiliate" shall specifically exclude [***].

(d) "Applicable Law" or "Law" means all applicable common law, laws, constitutional provisions, ordinances, statutes, rules, regulations, administrative rulings, executive orders and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, agency or other body, domestic or foreign, including but not limited to any applicable rules, regulations, guidelines, or other requirements of Governmental Authorities that may be in effect from time to time.

(e) "Applicable Rate" means as of any particular date, the prime rate as quoted in the Money Rates Section of *The Wall Street Journal*, plus [***]%.

(f) [***]

(g) "Business" means researching, developing, manufacturing, selling, marketing, distributing and using a system, process or reagents for the identification and/or quantitation of nucleic acids or the performance of services relating to any of the foregoing, as conducted by Ibis or by Isis, with respect to the Division, on and prior to the Closing Date.

(h) "Business Day" means any day other than a Saturday, Sunday, or a day on which the banks in Chicago, Illinois are authorized or obligated by Law to close.

(i) "Call Option" has the meaning ascribed to such term in the Call Option Agreement.

(j) "Call Option Agreement" means that certain Call Option Agreement, dated as of the Investment Date, by and among Isis, Ibis and AMI.

(k) "Capital Stock" means all capital stock, equity or controlling interests and other securities in an issuer, including, without limitation, options, warrants, depositary receipts, stock appreciation or phantom stock rights or other agreements or undertakings, including stock or securities convertible or exchangeable for any shares of capital stock, equity or controlling interests or other securities in an issuer or containing any profit participation features or pursuant to which such issuer is or could be bound to issue or repurchase any capital stock, equity or controlling interests or other securities.

(l) "Change of Control" means, with respect to any Person, the occurrence of (i) any consolidation or merger of such Person with or into any other Person, or any other corporate reorganization or transaction (including the acquisition of Capital Stock of such Person (or any rights to acquire, or securities convertible into or exchangeable for, any such Capital Stock)), whether or not such Person is a party thereto, in which the stockholders or equity-holders of such Person or other Persons controlling such Person immediately prior to such consolidation, merger, reorganization or transaction, own Capital Stock either (A) representing directly, or indirectly through one or more entities, less than fifty percent (50%) of the economic interests in or voting power of such Person or other surviving entity immediately after such

consolidation, merger, reorganization or transaction or (B) that does not directly, or indirectly through one or more entities, have the power to elect a majority of the entire board of directors or equivalent governing body of such Person or other surviving entity immediately after such consolidation, merger, reorganization or transaction or (ii) a sale, lease, license or other disposition of all or a material portion of the assets of such Person.

(m) "Claim" means any claim, lawsuit, demand, audit, investigation, charge, suit, hearing, notice of a violation, litigation, action, proceeding, order, judgment, grievance, or arbitration, whether civil, criminal, administrative or otherwise, whether at law or in equity, or any inquiry likely to result in any of the foregoing.

(n) "Code" means the Internal Revenue Code of 1986, as amended from time to time.

(o) "Common Stock" means the Common Stock of Ibis, par value $0.001 per share.

(p) "Confidential Information" means all information and any tangible embodiments thereof provided by or on behalf of the Disclosing Party to the Receiving Party or to the Receiving Party's Representatives either in connection with the discussions and negotiations pertaining to the Transaction Documents or in the course of performing the Transaction Documents, including without limitation: know-how; data; knowledge; practices; processes; research and development plans; engineering designs and drawings; research data; manufacturing processes and techniques; scientific, manufacturing, marketing and business plans; and financial and personnel matters relating to the Disclosing Party or to its present or future products, sales, suppliers, customers, employees, consultants, independent contractors, investors or business; regardless of whether any of the foregoing are marked "confidential" or "proprietary" or communicated to the other by the Disclosing Party in oral, written, graphic or electronic form. Notwithstanding the foregoing, information of a Party will not be deemed Confidential Information to the extent that the Receiving Party can show by competent proof that such information:

(i) is or becomes generally available to the public other than as a result of an unauthorized disclosure by the Receiving Party or its Representatives;

(ii) was available to the Receiving Party or its Representatives on a non-confidential basis prior to its disclosure by the Disclosing Party or its Representatives;

(iii) is or becomes available to the Receiving Party or its Representatives from a Person, other than the Disclosing Party or its Representatives, who is not bound by a confidentiality obligation to the Disclosing Party or its Representatives; or

(iv) is independently developed by the Receiving Party or its Representatives without reference to or use of any Confidential Information of the Disclosing Party.

(q) "Contract" means any contract, lease, deed, mortgage, license, instrument, note, commitment, undertaking, understanding, indenture, joint venture, purchase order, service order and all other agreements and arrangements, whether oral or written.

(r) "Contribution Agreement" means the Contribution Agreement, dated as of July 31, 2007, by and between Isis and Ibis.

(s) "Corporate Services Agreement" means that certain Corporate Services Agreement, dated as of July 31, 2007, by and between Isis and Ibis.

(t) "Division" means the Ibis Biosciences division of Isis.

(u) "Earnout Threshold" means $150 million minus all commercial revenue for the period beginning on the date [***] through the Closing Date as set forth on Schedule 1(u), which has been prepared in accordance with GAAP and Isis' internal controls and procedures for financial reporting.

(v) "Employee Pension Benefit Plan" has the meaning set forth in Section 3(2) of ERISA.

(w) "Employee Welfare Benefit Plan" has the meaning set forth in Section 3(1) of ERISA.

(x) "Encumbrance" means any mortgage, covenant, hypothecation, condition, Claim, easement, encroachment, right of way, restriction, option, lien (statutory or otherwise), pledge, charge, license, security interest or encumbrance of any nature whatsoever.

(y) "Environmental Laws" means any federal, state, local or foreign statutes, ordinances, codes, treaties, or other Laws (including, without limitation, the Comprehensive Environmental Response, Compensation, and Liability Act, the Resource Conservation and Recovery Act, the Clean Air Act, the Clean Water Act, the Toxic Substances Control Act, the Oil Pollution Prevention Act, the Federal Insecticide, Fungicide, & Rodenticide Act, the Safe Drinking Water Act, the Hazardous Materials Transportation Act, the Solid Waste Disposal Act, the Emergency Planning and Community Right-to-Know Act, the Occupational Safety and Health Act), including any regulations, rules, plans, other criteria, policies or guidelines promulgated pursuant to such Laws, and all common law, orders, judgments, decrees, judicial or agency interpretations now or hereafter in effect relating to pollution, the generation, production, installation, use, storage, treatment, transportation, Release, threatened Release, investigation, monitoring, remediation, cleanup, abatement, removal, or disposal of Hazardous Materials, noise control, odor or the protection of public or workplace health or safety, natural resources, or the environment.

(z) "ERISA" means the Employee Retirement Income Security Act of 1974, as amended.

(aa) "Escrow Agent" means LaSalle Bank National Association, a national banking association.

(bb) "Fundamental AMI Representations" means those representations and warranties of AMI set forth in Section 5.2(a) (Power and Authority), Section 5.2(b) (Enforceability), Section 5.2(c) (Governmental Authority; Consents), and Section 5.2(d) (No Conflicts).

(cc) "Fundamental Isis Representations" means those representations and warranties of Isis set forth in Sections 5.1(a) (Power and Authority), 5.1(b) (Enforceability), 5.1(c) (Governmental Authority; Consents), 5.1(d) (No Conflicts), 5.2(e) (Due Organization; Qualification), 5.1(g) (Capitalization; Voting Rights), 5.1(j) (Title to Properties and Tangible Assets; Liens, etc.), 5.1(k) (Sufficiency of Assets), 5.1(m) (Compliance with Other Instruments) and 5.1(v) (Brokers' Fees).

(dd) "GAAP" means United States generally accepted accounting principles, applied on a consistent basis.

(ee) "Governmental Authority" means any governmental or quasi-governmental agency, department, bureau, office, center, institute, court, commission or other unit of the government of the United States of America or of any of its respective States or local units of government thereof, or of a foreign sovereign or of a provincial, regional or metropolitan government thereof, including, without limitation, any Regulatory Authority.

(ff) "Grants Receivable" means (i) any payments due to Ibis from a Governmental Authority or not for profit Person with respect to grants awarded to Ibis or Contracts with Ibis, in each case to the extent Ibis has performed the research or other services described in the grant or Contract, but not received payment therefor as of the Closing and (ii) the rate reserves identified as "Government Rate Reserves" on Schedule 1(ff), which has been prepared in accordance with GAAP and Isis' internal controls and procedures for financial reporting.

(gg) "Hazardous Materials" means any substance, chemical, solvent, compound, waste, residue, contaminant or other material which is regulated by or forms the basis of liability now or hereafter under any Environmental Law, including, without limitation: (i) any "solid waste," "dangerous goods," "hazardous waste," "hazardous substance," "hazardous material," "extremely hazardous waste," "pollutant," "contaminant," "hazardous constituent," "special waste," "universal waste," "toxic substance," or any other similar term or phrase as defined under any Environmental Law; (ii) any petroleum, or petroleum products, byproducts or breakdown products, including crude oil and any fraction thereof; (iii) natural synthetic gas usable for fuel; (iv) any asbestos, lead-based paint, polychlorinated biphenyl, mold, radon gas, radioactive material or byproduct, isomer of dioxin, or any material or thing containing or composed of such substance or substances; and (v) any virus, bacteria, protozoa, parasite, fungi, or other pathogen or any other substance, chemical, solvent, compound, waste, residue, contaminant or other material which is hazardous, toxic, poisonous, reactive, corrosive or otherwise may present a threat to human health, safety, natural resources, wildlife or the environment.

(hh) "Ibis Employee Retention Amount" means $[***].

(ii) "Ibis Net Sales" means:

(i) the gross amount billed by Ibis or its Affiliates after the Closing for the sale or other transfer or disposition of Products to, or performance of Services for, non-Affiliate third parties in bona fide arms length transactions, less deductions for:

A. discounts, including cash discounts, customary trade allowances or rebates actually taken, and promotional discounts;

B. credits or allowances given or made for rejection, recall or return of previously sold Products and rebates for previously provided Services;

C. any Tax (including any Tax such as a value added or similar Tax) levied on the sale, transportation or delivery of Products when included on the invoice or other written document between the parties as payable by the purchaser and collectable by Ibis; and

D. freight, postage, transportation, insurance and duties on shipment of Product when included on the invoice or written document between the parties as payable by the purchaser and collectable by Ibis;

(ii) [***]; and

(iii) the amount of any [***].

Ibis Net Sales calculations shall be applied as provided above and modified as appropriate as follows:

1. When a Product is sold or licensed by Ibis or its Affiliates or a Service is provided to a non-Affiliate third party with whom Ibis or such Affiliate does not deal at arms length, Ibis Net Sales for that Product or Service shall equal an average of Ibis Net Sales for similar quantities of Products sold or Services provided within the same calendar quarter in an arms length transaction in the same geographic market and class of purchasers or Service recipients as the non-arms length purchaser or Service recipient.

2. In the event that a Product is sold or a Service provided in combination with any other product(s) or service(s), Ibis Net Sales with respect to the Product or Service of the combination shall be determined by the fraction A over A + B in which "A" is Ibis Net Sales of the Product or Service portion of the combination when sold separately during the applicable calendar quarter, and "B" is Ibis Net Sales of the other product(s) or service(s) of the combination product or service when sold separately during the applicable calendar quarter.

3. In the event a Product or Service is incorporated into a profile in which said Product or Service contributes only a small proportion of the value of the total package, but the adjustment set forth in paragraph 2, above is impractical or if similar quantities of product(s) are not sold or similar quantities of Services are not provided pursuant to paragraph 1, above, then the Parties

shall negotiate in good faith to establish an equitable adjustment to Ibis Net Sales for such Product or Service to fairly reflect the proportion of the value of the profile contributed by the Product or Service or the value of the Product or Service.

(jj) "Indebtedness" means (i) all indebtedness or other obligations of Ibis for borrowed money, whether current, short-term or long-term, secured or unsecured, and all accrued interest, premiums, penalties and other obligations relating thereto, (ii) all indebtedness of Ibis for the deferred purchase price of property or services which is not evidenced by accounts payable incurred in the ordinary course of business, (iii) all existing lease obligations of Ibis under leases which are capital leases in accordance with GAAP, (iv) any liability of Ibis under deferred compensation plans, phantom stock plans, severance or bonus plans, or any change in control or similar payment or increased cost which is triggered or made or will be made payable by Ibis as a result of the transactions contemplated hereby, other than the Permitted Employee Compensation Plan, (v) any off balance sheet financing of Ibis, (vi) any payment obligations of Ibis in respect of banker's acceptances or letters of credit, (vii) any liability of Ibis with respect to interest rate swaps, collars, caps and similar hedging obligations, (viii) all obligations of Ibis arising under or with respect to any conditional sale or other title retention agreement with respect to property acquired by Ibis, (ix) past due or deferred rent of Ibis, (x) the amount of accounts payable owed by Ibis to any Person that have not been paid within 45 days of the date of invoice thereof (xi) all "cut" but "uncashed" checks of Ibis outstanding as of the Closing, (xii) any indebtedness referred to above of any Person which is either guaranteed by, or secured by a security interest upon any property owned by, Ibis and (xiii) accrued and unpaid interest of, and prepayment premiums, penalties or similar contractual charges arising as a result of the discharge of any such foregoing obligation.

(kk) "Intellectual Property" means all of the following in any jurisdiction throughout the world: (i) patents, patent applications and patent disclosures and statutory invention registrations, including reissues, divisions, continuations, continuations in part, extensions and reexaminations thereof; (ii) trademarks, service marks, trade dress, trade names, corporate names, logos and slogans (and all translations, adaptations, derivations and combinations of the foregoing) and Internet domain names any and all common law rights and registrations and applications for the registration thereof, and all extensions and renewals of any of the foregoing; (iii) copyrights and copyrightable works (including Software), registered copyrights and copyright applications, mask works, net lists and schematics; (iv) confidential and proprietary information including technology, know-how, trade secrets, unpatented inventions, ideas, algorithms and processes (including, without limitation, manufacturing and production processes and techniques, drawings, specifications, designs, plans, proposals, test data including pharmacological, biological, chemical, biochemical, toxicological and clinical test data, analytical and quality control data, stability data and customer and supplier lists and related information); (v) other intellectual property and proprietary information and (vi) all copies and tangible embodiments of the foregoing, such as instruction manuals, laboratory notebooks, prototypes, samples, specimens, studies and summaries.

(ll) "Investment Date" means January 23, 2008.

(mm) "Investment Documents" means the Master Agreement, the Call Option Agreement, the Investor Rights Agreement **[**and the Stock Subscription Agreement**]**.

(nn) "Investor Rights Agreement" means that certain Investor Rights Agreement, dated as of the Investment Date, by and among Isis, Ibis and AMI.

(oo) "Isis Licensed Intellectual Property" means the Intellectual Property set forth on Schedule 1(qq).(1)

(pp) [***]

(qq) "Knowledge" and terms of similar meaning (including, without limitation, "is aware of") mean (i) with respect to Ibis and Isis, the actual knowledge of any of the individuals set forth on Schedule 1(qq), after due investigation, including, without limitation, inquiry of Persons with subject matter knowledge, *provided* that (A) solely for purposes of Sections 5.1(l)(v), 5.1(l)(vi) and 5.1(l)(ix), "Knowledge" and terms of similar meaning (including, without limitation, "is aware of") mean the actual knowledge of any employee of Ibis or Isis, after due investigation, including, without limitation, inquiry of Persons with subject matter knowledge and (B) solely for purposes of Section 5.1(l), inquiry of Persons with subject matter knowledge shall include inquiry of the outside counsel involved in the development or prosecution of the Business IP or who conducted 'freedom to operate analyses' identified on Schedule 1(qq) and (ii) with respect to AMI, the actual knowledge of any of the individuals set forth on Schedule 1(qq), after due investigation.

(rr) "Licenses" means all licenses, permits, certificates of authority, variances, authorizations, approvals, registrations, franchises, orders and similar consents issued by any Governmental Authority or other Person, provided that the term License shall not include any license or other right to use any Intellectual Property.

(ss) "Loss" means any loss, liability, demand, Claim, action, cause of action, cost, damage, diminution in value, deficiency, Tax, penalty, fine or expense (including interest, penalties, reasonable attorneys' fees and expenses and all amounts paid in investigation, defense or settlement of any of the foregoing and the enforcement of any related rights), whether or not arising out of third party claims.

(tt) "Management Presentations" means the Management Presentations of Ibis delivered to AMI pursuant to Section 2(h) of the Master Agreement.

(uu) "Master Agreement" means that certain Strategic Alliance Master Agreement, dated as of the Investment Date, by and among Isis, Ibis and AMI.

(vv) "Multiemployer Plan" has the meaning set forth in Section 3(37) of ERISA.

(ww) "Offering Memorandum" means the Offering Memorandum of Ibis, dated November 2006 as made available to AMI.

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(1) This will be the Isis Intellectual Property that Ibis Employees have identified as being useful to the Business.

(xx) [***] means any payments, including, but not limited to royalty payments, license fees and milestone payments that are made by non-Affiliate third parties to [***](or any of its Affiliates) in bona fide arms length transactions in consideration for one or more license or equivalent agreements that grant such non-Affiliate third party rights under any [***](i) make, have made, use, sell, offer for sale or import any products [***]to another party for a fee, in each case, where any of the foregoing conduct by such non-Affiliate third party in the absence of such rights under license or equivalent agreement would infringe (directly, contributorily, by inducement or otherwise), misappropriate or otherwise conflict with any [***]

(yy) "Permitted Employee Compensation Plan" means the compensation plan mutually agreed by the Parties regarding the [***] the terms of which are described on Exhibit D attached hereto.

(zz) "Permitted Encumbrances" means (i) liens for current property Taxes not yet due and payable, (ii) Encumbrances arising in connection with and solely as a result of Permitted Indebtedness and (iii) except with respect to Intellectual Property, other imperfections of title, restrictions or Encumbrances, if any, which imperfections, restrictions or Encumbrances do not, individually or in the aggregate, impair the continued use and operation of the assets used in the operation of the Business and do not affect the merchantability of the title to such assets to which they relate.

(aaa) "Permitted Indebtedness" means (i) accounts payable incurred in the ordinary course of business that are paid within forty-five (45) days of the date of invoice thereof, (ii) Indebtedness arising from existing and future lease obligations of Ibis under equipment leases that are capital leases in accordance with GAAP so long as the collateral for such capital leases is limited to the equipment acquired and the aggregate amount of such capital leases does not exceed $[***] and (iii) Indebtedness incurred pursuant to the Corporate Services Agreement or the Contribution Agreement.

(bbb) "Person" means an individual, a partnership, a corporation, an association, a limited liability company, a joint stock company, a trust, a joint venture, an unincorporated organization, or a Governmental Authority (or any department, agency, or political subdivision thereof).

(ccc) "Pre-Closing Tax Period" means a Tax period ending on or before the Closing Date and the portion through the end of the Closing Date for any Tax period that includes (but does not end on) the Closing Date.

(ddd) "Post-Closing Tax Period" means a Tax period beginning after the Closing Date and, for any Tax period that includes (but does not end on) the Closing Date, the portion of such period beginning after the Closing Date.

(eee) "Products" means the T5000 Biosensor System (including kits) and any Successor Products.

(fff) "Purchase Offer" means any proposal or offer from any Person (other than AMI and its Affiliates in connection with the transactions contemplated hereby) or any agreement or offer relating to any (i) reorganization, liquidation, dissolution, share exchange,

business combination or recapitalization of Ibis, (ii) merger or consolidation involving Ibis, (iii) purchase or sale of any assets or Capital Stock of Ibis (other than the purchase and sale of inventory and capital equipment in the ordinary course of business), (iv) distribution of Ibis' existing or future products, (v) licensing of any Business IP from Ibis or (vi) any other transaction or business combination involving Ibis or its business or assets which would reasonably be expected to interfere with, impede or materially delay the transactions contemplated by the Transaction Documents or dilute the benefits thereof to AMI and its Affiliates.

(ggg) "Real Property" means the Leased Real Property.

(hhh) "Regulatory Authority" means any Governmental Authority that has responsibility for granting any licenses or approvals or granting pricing and/or reimbursement approvals necessary for the marketing and sale of medical devices or diagnostic products, including without limitation, the FDA, the European Medicines Agency and the United States Department of Health and Human Services.

(iii) "Release" means any spilling, leaking, pumping, pouring, emitting, emptying, discharging, injecting, escaping, leaching, dumping, depositing, disposing or other release into the environment (including the abandonment or discarding of barrels, drums, containers or other closed

receptacles), including any dispersal, migration or other movement of any substance through or in air, soil, surface water, groundwater or property.

(jjj) "Representatives" means with respect to any Person, such Person's employees, directors, officers, Affiliates and authorized agents.

(kkk) "Schedule" means any of the Disclosure Schedules delivered to AMI herewith and incorporated herein pursuant to Section 10.11 hereof.

(lll) "SEC" or "Commission" means the United States Securities and Exchange Commission.

(mmm) "Securities Act" means the Securities Act of 1933, as amended.

(nnn) "Services" means using any Business IP to analyze samples containing nucleic acids and providing the results of such analyses to a third party for a fee.

(ooo) "Shares" means 114,251 shares of Common Stock issued to AMI pursuant to the Master Agreement, as may be held from time to time by AMI and its permitted assigns, representing approximately 10.25% of the issued and outstanding Common Stock.

(ppp) "Software" means any and all (i) computer programs, libraries, firmware and middleware, including any and all software implementations of algorithms, models and methodologies, whether in source code or object code, (ii) databases and compilations, including any and all data and collections of data, whether machine readable or otherwise, (iii) descriptions, flow-charts and other work product used to design, plan, organize and develop any of the foregoing and (iv) all programmer and user documentation, including user manuals and training materials, relating to any of the foregoing.

(qqq) **[**"Stock Subscription Agreement" means the Stock Subscription Agreement dated as of **[ ]**, 2008, by and among Ibis, Isis and AMI.**]**

(rrr) "Subsidiary" means, with respect to a Person, any corporation, limited liability company, partnership, association or other business entity of which (i) if a corporation, a majority of the total voting power of shares of stock entitled (without regard to the occurrence of any contingency) to vote in the election of directors, managers or trustees thereof is at the time owned or controlled, directly or indirectly, by such Person or one or more of the other Subsidiaries of such Person or a combination thereof, or (ii) if a limited liability company, partnership, association or other business entity, a majority of the partnership or other similar ownership interest thereof is at the time owned or controlled, directly or indirectly, by such Person or one or more Subsidiaries of such Person or a combination thereof. For purposes hereof, a Person shall be deemed to have a majority ownership interest in a limited liability company, partnership, association or other business entity if such Person shall be allocated a majority of limited liability company, partnership, association or other business entity gains or losses or shall be or control any managing director or general partner of such limited liability company, partnership, association or other business entity.

(sss) "Successor Products" means any product that (i) relies upon [***] and determination of [***] by [***] using either the Ibis [***], each as in existence in the Business at the Closing, including as may be modified subsequently by AMI or (ii) is described in U.S. Patent No.'s [***].

(ttt) "T5000 Biosensor System" means the biosensor platform generally known as the T5000 Biosensor System, together with all equipment, hardware, Software, systems and other materials required for its use, or provided or recommended by Ibis, Isis or any of their respective Affiliates for its use, as well as all prior versions of the T5000 Biosensor System, including such systems known as "TIGER."

(uuu) "Tax" means any federal, state, local, or foreign income, gross receipts, license, payroll, employment, excise, severance, stamp, occupation, premium, windfall profits, environmental, customs and other duties, capital stock, franchise, profits, withholding, social security, unemployment, disability, real property, personal property, sales, use, transfer, registration, value added, alternative or add-on minimum, estimated, or other tax of any kind whatsoever, including any interest, penalty, or addition thereto, whether disputed or not, and including any obligation to indemnify or otherwise assume or succeed to the Tax liability of any other Person.

(vvv) "Tax Return" means any return, declaration, report, claim for refund, or information return or statement relating to Taxes, including any schedule or attachment thereto, and including any amendment thereof.

(www) "Third Party Payments" means payments, including, but not limited to damage awards, royalty payments, license fees and milestone payments, that are made by[***]to a third party, which are based upon making, having made, using, selling, offering for sale or importing [***]under order of a Governmental Authority or license agreements or equivalent agreements with the third party to obtain rights under any United States or foreign

copyrights, patent applications or patents that are [***]to make, have made, use, sell, offer for sale or import any [***]

(xxx) "Transaction Documents" means the Master Agreement, the Investor Rights Agreement, **[**the Stock Subscription Agreement, **]** the Call Option Agreement, the Transition Services Agreement, the Escrow Agreement and this Agreement.

(yyy) "Transfer" means, with respect to Capital Stock, any sale, pledge, hypothecation, assignment, Encumbrance or other transfer or disposition, whether directly, indirectly, voluntarily, involuntarily, by operation of Law, pursuant to judicial process or otherwise and, when the context so requires, the act of doing any of the foregoing.

Section references for definitions of defined terms defined in the body of this Agreement rather than in this Section 1.

Defined Term	Section
"§ 338(h)(10) Election"	8.6(g)
"Abbott"	Preamble
"ADR"	10.8
"Agreement"	Preamble
"AMI"	Preamble
"AMI Group"	8.2(a)
"AMI Proceeding"	8.6(e)(ii)
"Applicable AMI Proceeding"	8.6(e)(ii)
"Closing"	3.1
"Closing Date"	3.1
"Closing Purchase Price"	2.2
"Disclosing Party"	8.8(a)
"Disclosure Schedules"	Section 5
"Earnout Payments"	2.3(e)
"Earnout Period"	2.3(a)
"Escrow Agreement"	4.1(l)
"Financial Statements"	5.1(t)
"Foreign Person"	4.1(m)
"Government Contracts"	5.1(l)(ii)
"HSR Act"	4.1(d)
"Ibis"	Preamble

"Ibis Contracts"	5.1(x)(i)
"Ibis Employees"	8.11(a)
"Indemnified Party"	8.2(e)
"Indemnifying Party"	8.2(e)
"Isis"	Preamble
"Isis Proceeding"	8.6(e)(i)
"Isis Retirement Plans"	8.11(d)
"Leased Real Property"	5.1(w)(ii)
"Leasehold Improvements"	5.1(w)(ii)
"Leases"	5.1(w)(ii)
"Material Adverse Effect"	4.1(j)
"Material Licenses"	5.1(q)(ii)
"Noncompete Period"	8.9(a)
"Nonsolicitation Period"	8.9(c)
"Parties"	Preamble
"Party"	Preamble
"Purchase Price"	2.2
"Receiving Party"	8.8(a)
"Remaining Shares"	Recitals
"Restricted Assets"	2.4
"Seller Group"	8.2(b)
"Straddle Period"	8.6(c)(ii)
"Third Party Claim"	8.2(e)
"Transaction Value"	2.2
"Transition Services Agreement"	4.1(k)
"WARN Act"	8.11(b)

Section 2. BASIC TRANSACTION; PURCHASE PRICE.

2.1 Sale and Transfer of the Remaining Shares. Subject to the terms and conditions of this Agreement, at the Closing, Isis shall sell, convey, assign, transfer and deliver to AMI all of the Remaining Shares, free and clear of all Encumbrances, and AMI shall purchase, acquire and accept the Remaining Shares from Isis.

2.2 Purchase Price. The purchase price (the "Purchase Price") for the Remaining Shares shall be equal to (i) $[ ](2) (the "Transaction Value"), minus (ii) the amount of any Indebtedness of Ibis as of the Closing (not including the amount of any Indebtedness that is Permitted Indebtedness under clauses (i) or (ii) of the Permitted Indebtedness definition), minus (iii) the Ibis Employee Retention Amount, plus (iv) the Earnout Payments. The "Closing Purchase Price" is an amount equal to (x) the Transaction Value, minus (y) the amount of any Indebtedness of Ibis as of the Closing (not including the amount of any Indebtedness that is Permitted Indebtedness under clauses (i) or (ii) of the Permitted Indebtedness definition), minus (z) the Ibis Employee Retention Amount.

2.3 Earnout Payments.

(a) Subject to Sections 2.3(e) and 2.3(f), from and after the Closing Date until December 31, 2025 (the "Earnout Period"), Ibis will pay to Isis an amount equal to five percent (5%) (the "Earnout Rate") of cumulative Ibis Net Sales that are (i) in excess of the Earnout Threshold and

(ii) less than or equal to $2.1 billion. Such amounts payable to Isis will be reduced by an amount equal to [***]% of any [***], but in no event will such amounts for such Ibis Net Sales be less than two and a half percent (2.5%) of such cumulative Ibis Net Sales.

(b) For cumulative Ibis Net Sales that are in excess of $2.1 billion, the Earnout Rate will reduce from 5% to 3%. The corresponding amounts payable to Isis will be reduced by an amount equal to [***]% of any [***], but in no event will such amounts for such Ibis Net Sales be less than one and a half percent (1.5%) of such cumulative Ibis Net Sales.

(c) In calculating the amount of any reduction to the earn-out payments permitted by the second sentence of either Section 2.3(a) or Section 2.3(b) that result from any [***] that are [***], the amount of such [***] will be [***] of the Earnout Period from the date of such [***]. For example, if Ibis makes a [***] in the form of [***] equal to [***] to [***] which, in AMI's reasonable judgment was [***] and such [***] was made in 2015, then, in each calendar quarter, Ibis would be able to reduce the corresponding amounts payable for such quarter by [***], in each case subject to the applicable 2.5% or 1.5% floor under Section 2.3(a) or Section 2.3(b).

(d) The earnout amounts described in Sections 2.3(a) and 2.3(b) will be payable on a quarterly basis, within [***] days after the last day of each calendar quarter, by wire transfer of immediately available funds to an account designated by Isis. Within [***] days of the end of each calendar quarter, Ibis will deliver to Isis its non-binding, preliminary, good faith estimate of Ibis Net Sales for such calendar quarter. All amounts included in Ibis Net Sales shall be in United States funds collectible at par in Chicago, Illinois. With respect to product or service revenues, [***], or [***] that are used in the calculation of Ibis Net Sales and are in monies other than United States dollars, the amount to be used will first be determined in the foreign currency of the country for such monies and then converted into equivalent United States

(2) The Transaction Value from the Option Notice to be inserted here.

funds using the same conversion methodology that Abbott uses to prepare its financial statements filed with the SEC.

(e) Notwithstanding the foregoing, Sections 2.3(a) through 2.3(c), (i) the earnout amounts described in Sections 2.3(a) and 2.3(b) will be payable only on cumulative Ibis Net Sales in excess of the Earnout Threshold, (ii) no such earnout amounts will be payable in any calendar year in which total Ibis Net Sales in such calendar year were less than or equal to $[***] million, (iii) in any calendar year in which Ibis Net Sales exceed $[***] million and cumulative Ibis Net Sales exceed the Earnout Threshold, the earnout amounts described in Sections 2.3(a) and 2.3(b) will be payable with respect to all Ibis Net Sales in such calendar year which are in excess of the Earnout Threshold and (iv) all Ibis Net Sales, regardless of whether earnout amounts are payable thereon, will be included in cumulative Ibis Net Sales for purposes of determining the applicable Earnout Rate. For example, if Ibis Net Sales in each of the calendar years 1 and 3 are equal to $[***] million and Ibis Net Sales in each of the calendar years 2 and 4 are equal to $[***] million, no earnout amounts would be payable in calendar years 1 through 3, but earnout amounts would be payable with respect to the entire $[***] million in Ibis Net Sales in calendar year 4. The earnout amounts payable by Ibis to Isis pursuant to this Section 2.3 are referred to herein as the "Earnout Payments."

(f) Ibis shall maintain its books and records used to determine Ibis Net Sales, [***], and [***] for a period of three (3) years from the date of the Earnout Payment to which they pertain. Ibis shall make such books and records available for inspection by third party representatives of Isis approved in writing (which approval shall not be unreasonably withheld, conditioned or delayed) once per calendar year at reasonable times and upon reasonable written advance notice from Isis. All information contained in these books and records shall be Confidential Information and will be used only for the purpose of determining the accuracy of Ibis' calculation of any Earnout Payment.

(g) Notwithstanding any provision of this Agreement or any other Transaction Document, except with respect to any [***] arising as a result of or in connection with a breach of the representations and warranties set forth in Section 5.1(l)(v), the Earnout Payment reductions set forth in Sections 2.3(a) and 2.3(b) will be the AMI Group's sole and exclusive remedy for any [***].

2.4 Restricted Assets. Notwithstanding any other provision in this Agreement to the contrary, this Agreement shall not constitute an agreement to assign or transfer any interest in any Contract, asset, claim, right or benefit the assignment or transfer of which is otherwise contemplated by the transactions contemplated by this Agreement to the extent such assignment or transfer (or attempt to make such an assignment or transfer) without the consent or approval of a third party would constitute a breach or other contravention of the rights of such third party, or affect adversely the rights of any Party or their Affiliates thereunder (such assets being collectively referred to herein as "Restricted Assets"). Any assignment or transfer of a Restricted Asset shall be made subject to such consent or approval being obtained. If any such consent or approval is not obtained prior to the Closing, (i) the assigning or transferring Party shall continue to use its commercially reasonable efforts to cooperate with the other Party in attempting to obtain any such consent or approval and (ii) establish alternative arrangements (such as a license, sublease, subcontract or operating agreement) until such time as such consent

or approval has been obtained which results in the assignee or transferee Party receiving all the benefits and bearing all the burdens with respect to any such Restricted Asset (subject to Section 8.4, pursuant to which Isis shall be liable for and pay all out-of-pocket costs and expenses associated with obtaining third party consents associated with any Ibis Contract or Restricted Asset in excess of $[***] in the aggregate).

Section 3. CLOSING OF THE TRANSACTION.

3.1 The Closing. Subject to the satisfaction or waiver of the conditions set forth herein, the closing of the transactions contemplated by this Agreement (the "Closing") shall take place at the offices of Kirkland & Ellis LLP in Chicago, Illinois, at 10:00 a.m. local time on or before the third Business Day following the satisfaction or waiver of all conditions to the obligations of the Parties to consummate the transactions contemplated herein, or such other time and place as the Parties may mutually determine (the "Closing Date"), and the Closing shall be deemed effective as of 12:01 a.m. local time on the Closing Date.

3.2 Deliveries at the Closing. At the Closing:

(a) Isis shall deliver to AMI (i) the various certificates, agreements, instruments and documents referred to in Section 4.1 below and (ii) such other instruments of sale, transfer, conveyance and assignment as AMI reasonably may request;

(b) AMI shall deliver to Isis (i) the Closing Purchase Price, via wire transfer of immediately available funds to an account designated in writing by Isis at least five (5) Business Days prior to the Closing Date, and (ii) the various certificates, agreements, instruments and documents referred to in Section 4.2 below;

(c) AMI shall deliver to the Escrow Agent the Ibis Employee Retention Amount, via wire transfer of immediately available funds to an account designated by the Escrow Agent, to be held in escrow pursuant to the terms of the Escrow Agreement;

(d) Isis shall deliver to Ibis all books, records and other materials of Ibis or related to or used by Ibis in the Business (unless otherwise specifically set forth in the Transition Services Agreement);

(e) Isis shall deliver to AMI the Permitted Employee Compensation Plan; and

(f) Isis shall deliver to AMI one or more compact discs or other electronic media containing the contents of the electronic dataroom maintained by Isis at [***] as of the date that is three Business Days prior to the date hereof, together with a certificate of an authorized officer certifying that such compact discs contain true, accurate and complete copies of the materials in such dataroom as of such date.

Section 4. CONDITIONS TO OBLIGATION TO CLOSE.

4.1 Conditions to Obligation of AMI. The obligation of AMI to consummate the transactions to be performed by it in connection with the Closing is subject to satisfaction of the following conditions:

(a) The representations and warranties of Isis set forth in this Agreement shall be true and correct in all material respects at and as of the date hereof and as of the Closing Date (disregarding any materiality or Material Adverse Effect qualifications contained therein); provided, that any representation or warranty of Isis set forth in this Agreement that is made as of any date other than the date hereof shall be true and correct as of such date in all material respects (disregarding any materiality or Material Adverse Effect qualifications contained therein).

(b) Each of Isis and Ibis shall have performed and complied in all material respects with all of their covenants hereunder through the Closing.

(c) No Claim shall be pending before any court, arbitrator, other body or administrative agency of any Governmental Authority wherein an unfavorable injunction, judgment, order, decree, ruling or charge would prevent consummation of any of the transactions contemplated by this Agreement (and no such injunction, judgment, order, decree, ruling or charge shall be in effect).

(d) All filings with and authorizations and approvals of Governmental Authorities that are required for the consummation of the transactions contemplated hereby shall have been duly made and obtained on terms reasonably satisfactory to AMI. Without limiting the generality of the foregoing, all applicable waiting periods (and any extensions thereof) under the Hart Scott Rodino Antitrust Improvements Act of 1976, as amended (the "HSR Act"), shall have expired or otherwise been terminated.

(e) Isis shall have delivered to AMI (i) a certificate from an officer of Isis to the effect that each of the conditions specified in Section 4.1(a), Section 4.1(b) and Section 4.1(j) is satisfied in all respects, (ii) a copy of the resolutions of the governing body of each of Isis and Ibis approving the transactions contemplated by this Agreement, certified by an officer of each of Isis and Ibis, respectively, (iii) certificates from appropriate authorities, dated as of or about the Closing Date, as to the good standing and qualification to do business of Ibis in its jurisdiction of incorporation, (iv) such other documents or instruments as are required to be delivered at the Closing pursuant to the terms hereof and (v) such other documents or instruments as AMI reasonably requests to effect the transactions contemplated hereby.

(f) Isis shall tender to AMI a certificate representing the Remaining Shares duly and validly endorsed for transfer in favor of AMI or accompanied by a separate stock power duly and validly executed by Isis and otherwise sufficient to vest in AMI legal and beneficial ownership of the Remaining Shares.

(g) Isis shall have received and delivered to AMI all third party consents identified on Schedule 4.1(g) and Isis and AMI shall have received all other

authorizations, consents, and approvals of Governmental Authorities referred to in Sections 5.1(c) and 5.1(d).

(h) Ibis shall have the benefit of all Licenses necessary to conduct the Business as it had been conducted prior to the Closing and as contemplated to be conducted immediately thereafter.

(i) Isis shall have obtained (A) payoff letters for any Indebtedness of Ibis to be paid by AMI on behalf of Isis at the Closing and (B) releases of any and all Encumbrances on the Remaining Shares or the assets of Ibis (except, with respect to the assets of Ibis, Permitted Encumbrances), all on terms reasonably satisfactory to AMI.

(j) Since the Investment Date, there shall have been no occurrence or disclosure of any event, circumstance or state of facts which has, or would reasonably be expected to have, a material adverse effect on the business, assets, condition (financial or otherwise), operations, operating results, employee relations, customer relations or supplier relations of Ibis (a "Material Adverse Effect").

(k) Isis and Ibis shall have executed and delivered to AMI the Transition Services Agreement substantially in the form attached hereto as Exhibit A (the "Transition Services Agreement") and the Transition Services Agreement shall be in full force and effect.

(l) Isis shall have executed and delivered to AMI an escrow agreement substantially in the form attached hereto as Exhibit B (the "Escrow Agreement") and the Escrow Agreement shall be in full force and effect.

(m) Isis shall have executed and delivered to AMI a non-foreign affidavit dated as of the Closing Date and in form and substance required under the Treasury Regulations issued pursuant to Section 1445 of the Internal Revenue Code stating that Isis is not a "Foreign Person" as defined in Code § 1445.

(n) There shall not have been any material breach of any of the terms and provisions of the Transaction Documents that has not been waived by AMI.

(o) Except as contemplated by Section 2.4 and the Transition Services Agreement, Ibis shall be entitled to fully exercise without restriction or limitation all legal and beneficial rights under the Ibis Contracts (including the Government Contracts) and all other assets, properties and rights related to, used in or necessary to operate and conduct the Business in all respects in the manner conducted on and prior to the Closing Date and as contemplated to be conducted from and after the Closing Date.

(p) [***].

AMI may waive any condition specified in this Section 4.1 if it executes a writing so stating at or prior to the Closing. In the event of any such waiver, AMI shall be deemed to have waived any claim against Isis for failure to satisfy such condition; *provided* that, except to the extent specifically and expressly set forth in such waiver, any such waiver shall not limit

AMI's right to recovery hereunder for a breach by either Isis or Ibis of any other provision of this Agreement.

4.2 Conditions to Obligation of Isis. The obligation of Isis to consummate the transactions to be performed by it in connection with the Closing is subject to satisfaction of the following conditions:

(a) The representations and warranties of AMI set forth in this Agreement shall be true and correct in all material respects at and as of the date hereof and as of the Closing Date.

(b) AMI shall have performed and complied in all material respects with all of its covenants hereunder through the Closing;

(c) No Claim shall be pending before any court, arbitrator, other body or administrative agency of any Governmental Authority wherein an unfavorable injunction, judgment, order, decree, ruling or charge would prevent consummation of any of the transactions contemplated by this Agreement (and no such injunction, judgment, order, decree, ruling or charge shall be in effect).

(d) All filings with and authorizations and approvals of Governmental Authorities that are required for the consummation of the transactions contemplated hereby shall have been duly made and obtained on terms reasonably satisfactory to Isis. Without limiting the generality of the foregoing, all applicable waiting periods (and any extensions thereof) under the HSR Act shall have expired or otherwise been terminated.

(e) AMI shall have delivered to Isis a certificate of AMI to the effect that each of the conditions specified above in Section 4.2(a) and Section 4.2(b) is satisfied in all respects.

(f) AMI shall have executed and delivered to Isis the Escrow Agreement and the Escrow Agreement shall be in full force and effect.

(g) AMI (and any other Abbott Holders (as defined in the Investor Rights Agreement)) shall have executed and delivered to Isis a written consent in form reasonably satisfactory to AMI and Isis, consenting to the transactions contemplated by Section 7.10.

Isis may waive any condition specified in this Section 4.2 if it executes a writing so stating at or prior to the Closing. In the event of any such waiver, Isis shall be deemed to have waived any claim against AMI for failure to satisfy such condition; *provided* that, except to the extent specifically and expressly set forth in such waiver, any such waiver shall not limit Isis' right to recovery hereunder for a breach by AMI of any other provision of this Agreement.

Section 5 REPRESENTATIONS AND WARRANTIES.

5.1 Representations and Warranties of Isis. As a material inducement to AMI to enter into this Agreement, except as set forth in the corresponding Section of the Disclosure

Schedules delivered to AMI herewith on the date hereof (the "Disclosure Schedules"), Isis hereby represents and warrants the following representations and warranties are as of the date hereof, and will be as of the Closing Date, true and correct:

(a) Power and Authority. Each of Ibis and Isis (i) has the power, authority and the legal right to enter into each of the Transaction Documents and to perform its obligations hereunder and thereunder, and (ii) has taken all necessary action required to authorize the execution and delivery of each of the Transaction Documents and the performance of its obligations hereunder and thereunder.

(b) Enforceability. Each of the Transaction Documents has been duly executed and delivered on behalf of Ibis and Isis and constitutes a legal, valid and binding obligation of each such Party and is enforceable against each such Party in accordance with its terms subject to the effects of bankruptcy, insolvency or other Laws of general application affecting the enforcement of creditor rights.

(c) Governmental Authority; Consents. All necessary consents, approvals and authorizations of all Governmental Authorities and other parties required to be obtained by Ibis and Isis in connection with the execution and delivery of each of the Transaction Documents and the performance of their obligations hereunder and thereunder have been obtained.

(d) No Conflicts. The execution and delivery of each of the Transaction Documents by each of Ibis and Isis and the performance of each such Party's obligations hereunder and thereunder, with or without the passage of time or giving of notice, (1) do not and will not conflict with or violate any requirement of Applicable Law or any provision of the certificate of incorporation, bylaws or any similar instrument of such Party, as applicable (2) do not and will not require any notice, conflict with, violate, or breach or constitute a default or require any consent or give rise to any termination or acceleration right or the creation of any Encumbrance on the Shares, the Additional Shares or the Remaining Shares or any of the properties or assets of Ibis under, any contractual obligation by which such Party is bound or subject to and (3) do not and will not cause the suspension, revocation, impairment, forfeiture or nonrenewal of any License applicable to Ibis, the Business or any of Ibis' operations, assets or properties.

(e) Due Organization; Qualification. Each of Ibis and Isis is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, with full corporate power and authority to enter into each of the Transaction Documents. Except as would not reasonably be expected to have a Material Adverse Effect, Ibis has obtained and currently maintains all qualifications to do business as a foreign corporation in all jurisdictions in which the character of the Business requires it to be so qualified. Ibis has all requisite power and authority and all authorizations and Licenses necessary to own, operate or conduct the Business.

(f) Subsidiaries. Ibis does not own or control any Capital Stock or other interest of any Person. Ibis is not a participant in any joint venture, partnership, limited liability company or similar arrangement. Since its inception Ibis has not merged with, acquired all or substantially all of the assets of (except pursuant to the Contribution Agreement) or acquired the Capital Stock of or any interest in any Person. Ibis does not hold the right to acquire any Capital

Stock or interest in any other Person or have any obligation to make any investment in any Person and no such rights, Capital Stock or interests are necessary for the operation of the Business. Isis does not control or possess the power, directly or indirectly to control the management, actions or policies of Regulus Therapeutics, LLC.

(g) Capitalization; Voting Rights.

(i) The authorized Capital Stock of Ibis consists of 1,228,501 shares of Common Stock, par value $0.001 per share, **[**1,114,251**]** shares of which are issued and outstanding, 1,000,000 of which are held by Isis (the "Remaining Shares") **[**and 114,251 shares of which are held by AMI**]**.

(ii) The issued and outstanding Capital Stock of Ibis as of the Closing will consist exclusively of the Shares**[**, the Additional Shares**]** and the Remaining Shares. Except as set forth in the Investor Rights Agreement, Ibis does not have any obligations to issue or redeem any shares of Capital Stock **[**, other than with respect to the Additional Shares**]** and Ibis has not issued any Capital Stock other than the Shares, **[**the Additional Shares**]** and the Remaining Shares. No Capital Stock issued by Ibis is listed on any stock exchange or unregulated market. Other than the Transaction Documents, there are no agreements with Isis or Ibis or any other Person with respect to the voting or Transfer of the Remaining Shares.

(iii) The Remaining Shares are: (A) duly authorized, validly issued, fully paid and nonassessable; (B) issued in compliance with all applicable state and federal Laws concerning the issuance of Capital Stock; and (C) free and clear of all Encumbrances other than the Call Option; *provided*, that the Remaining Shares may be subject to restrictions on Transfer under state and/or federal securities Laws as set forth herein or as otherwise required by such Laws at the time a Transfer is proposed.

(iv) The sale of the Remaining Shares to AMI hereunder is not subject to any preemptive rights, rights of first refusal or similar rights.

(h) Agreements; Liabilities.

(i) There are no judgments, orders, writs or decrees to which Ibis or Isis is a party currently pending or, to Isis' or Ibis' Knowledge, threatened which would prevent Ibis or Isis from entering into the Transaction Documents or issuing or Transferring the Remaining Shares pursuant to the terms of the Transaction Documents.

(ii) Ibis has not (A) accrued, declared or paid any dividends, or authorized or made any distribution upon or with respect to any class or series of its Capital Stock, (B) incurred or guaranteed any Indebtedness (other than Permitted Indebtedness), (C) made any loans or advances to any Person, other than advances for reasonable travel expenses to Ibis employees in the ordinary course of business, or (D) sold, exchanged, licensed or otherwise disposed of any of its tangible assets, other than the sale of its inventory in the ordinary course of business.

(iii) Ibis has no material obligations or liabilities (whether accrued, absolute, or to Isis' or Ibis' Knowledge contingent, unliquidated or otherwise, whether due or to become due and regardless of when or by whom asserted), including, without limitation, Taxes, except (A) obligations under the Ibis Contracts made available to AMI or under Contracts entered into in the ordinary course of business which, because of the dollar thresholds set forth in Sections 5.1(l) and 5.1(x), are not required pursuant to Sections 5.1(l) and 5.1(x) below to be described on Schedules 5.1(l) or 5.1(x) (but not liabilities for breaches of any such Contracts), (B) liabilities reflected on the Most Recent Balance

Sheet, (C) liabilities and obligations which have arisen after the date of the Most Recent Balance Sheet in the ordinary course of business (none of which is material or is a liability for breach of contract, tort, infringement (directly, contributorily, by inducement or otherwise), Claim or warranty (other than warranty claims arising in the ordinary course of business in connection with the sale of Products or under Ibis Contracts made available to AMI, none of which warranty claims individually or in the aggregate would reasonably be expected to have a Material Adverse Effect) and (D) other liabilities and obligations to the extent expressly disclosed in Schedule5.1(h)(iii).

(i) Obligations to Related Parties. There are no obligations of Ibis to Affiliates, officers, directors or employees of Ibis or Isis other than (A) for payment of salary to employees of Ibis for services rendered in the ordinary course of business, (B) reimbursement to employees of Ibis for reasonable expenses incurred in the ordinary course of business on behalf of Ibis, (C) standard employee benefits made generally available to all employees, pursuant to the Plans described on Schedule 5.1(p)(ii), (D) the Permitted Employee Compensation Plan or (E) Ibis' rights and obligations to Isis under the Contribution Agreement and Corporate Services Agreement. To Isis' and Ibis' Knowledge, all of the Contracts to which Ibis is a party or by which the Business or any of its assets is bound have been negotiated on an arms length basis.

(j) Title to Properties and Tangible Assets; Liens, Etc. Ibis has good and marketable title to its properties and tangible assets and good and valid title to its leasehold estates, in each case subject to no Encumbrance other than (i) Permitted Encumbrances and (ii) rights of the U.S. federal government in certain equipment purchased using government funds, as set forth on Schedule 5.1(j). The tangible assets of Ibis have been maintained in accordance with normal industry practice and are in good operating condition and repair (except for ordinary wear and tear).

(k) Sufficiency of Assets.

(i) Except for the services, funding and facilities provided under the Corporate Services Agreement, Ibis has all assets, properties and rights used in or necessary to operate or conduct the Business in all respects.

(ii) Except the services, funding and facilities provided under the Corporate Services Agreement and indirectly, via the Remaining Shares, Isis and its Affiliates do not have any right, title or interest in or to any asset, property, title or interest that is used in or necessary to operate or conduct the Business as conducted on and prior to the Closing Date or as contemplated to be conducted by Ibis and Isis after the Closing Date as reflected in the Offering Memorandum and Management Presentations.

Pursuant to the Contribution Agreement, Isis has transferred to Ibis all assets, properties and rights Isis owned or which are or were used in or necessary to operate or conduct the Business except the services, funding and facilities provided under the Corporate Services Agreement. No person employed by the Division prior to the date of the Contribution Agreement is currently employed by Isis and no former employee of Ibis or the Division is or has been employed by Isis.

(l) Intellectual Property.

(i) Schedule 5.1(l)(i) sets forth a complete and correct list of all of the following Intellectual Property used in or necessary to operate or conduct the Business (whether owned by Ibis or any other Person), and indicates with respect to each item, whether Ibis owns or licenses such Intellectual Property and the owner of any Intellectual Property covered by such license: (A) patented or registered Intellectual Property and pending patent applications or other applications for registrations of Intellectual Property (including jurisdiction, registration and application number, as applicable, and record owner), (B) registered and material unregistered trademarks, service marks, trade names, and Internet domain names, (C) Software (other than unmodified, commercially available, off-the-shelf Software purchased or licensed for less than an individual cost of $[***] and a total cost of $[***] in the aggregate for all such licenses), (D) material algorithms embodied in the Products and any other material trade secrets; and (E) all other material Intellectual Property used in or necessary to operate or conduct the Business (including, without limitation, all Intellectual Property set forth or required to be set forth in the following Schedules to the Contribution Agreement: Schedule 2.1 (Ibis Business Assets), Schedule 2.2 (Ibis Business Patents), Schedule 2.5 (Ibis Trademarks) and Schedule 2.6 (Ibis Business Software)) (all Intellectual Property described in the foregoing, (A) through (E), collectively, (without regard to whether such Intellectual Property is set forth on Schedule 5.1(l)(i)) "Business IP").

(ii) Schedule 5.1(l)(ii) sets forth a complete and correct list of all of the following Contracts (other than licenses for unmodified, commercially available, off-the-shelf Software purchased or licensed for less than an individual cost of $[***] and a total cost of $[***] in the aggregate for all such licenses) relating to the Business IP (collectively, the "IP Contracts"): (A) Contracts in which Ibis or Isis or any of their respective Affiliates is a licensee or sublicensee of Business IP; (B) Contracts in which Ibis or Isis or any of their respective Affiliates is a licensor or sublicensor of Business IP; (C) Contracts to which Ibis or Isis or any of their respective Affiliates is a party, or by which any of the Business IP is bound, that give any third party any right, title or interest in or to any such Business IP; (D) Contracts with any Governmental Authority wherein any portion of the Business IP was developed or used ("Government Contracts"); and (E) Contracts that restrict Ibis' rights in or use or disclosure of Business IP.

(iii) Ibis owns and possesses all right, title and interest in and to, free and clear of all Encumbrances (other than the rights of Governmental Authorities under Government Contracts identified in Schedule 5.1(l)(iii) to the Intellectual Property identified in such Schedule) or has a valid and enforceable license to use (pursuant to a

written license agreement set forth and described in Schedule 5.1(l)(ii) or a written license for unmodified, commercially available, off-the-shelf Software purchased or licensed for less than an individual cost of $[***] and a total cost of $[***] in the aggregate) the Business IP.

(iv) Neither Isis nor any of its Affiliates (other than Ibis) has any right, title or interest in or to any of the Business IP.

(v) To Isis' or Ibis' Knowledge, neither Ibis, nor with respect to the Business, Isis, has infringed (directly, contributorily, by inducement or otherwise), misappropriated or otherwise conflicted with, and the operation of the Business (including the

development, manufacture and commercialization of the T5000 Biosensor System (including the [***] and [***]) and the assay kits specifically listed in the [***] [***]) does not and will not infringe (directly, contributorily, by inducement or otherwise), misappropriate or otherwise conflict with, the patents, trademarks, copyrights or trade secrets of any Person, and neither Ibis nor Isis is aware of any facts that indicate a likelihood of any of the foregoing (including without limitation, oral or written demands or offers to license any Intellectual Property from any Person). With respect to whether the operation or conduct of the Business has or will infringe (directly, contributorily, by inducement or otherwise), misappropriate or otherwise conflict with patent, trademark, copyright or trade secrets of any Person (other than Ibis or Isis or their respective Affiliates), the Parties hereto are relying upon the representations and warranties contained in this Section 5.1(l)(v) and not the representations and warranties contained in Sections 5.1(k)(i), 5.1(l)(viii) or 5.1(l)(ix).

(vi) All of the Business IP is valid and to Isis' or Ibis' Knowledge enforceable. Isis and Ibis have taken all necessary actions to maintain and protect all of the Business IP, including, without limitation, entering into confidentiality agreements with each of its employees, consultants and independent contractors, and customers and vendors as necessary so as not to adversely affect the validity or enforceability thereof and have complied with disclosure requirements as provided by any Government Contract. Neither Ibis nor Isis has disclosed any source code for any Software included in the Business IP to any Person in a manner that would impair the trade secret or other Intellectual Property protection of such source code. There are no claims, oppositions or cancellation proceedings that either were made or brought within the past [***] years, or are presently pending or, to Isis' or Ibis' Knowledge, threatened, against either Ibis or Isis contesting the validity, use, ownership, enforceability or registrability of any Business IP. Neither Ibis nor Isis is aware of any basis for any such claim, opposition or cancellation proceeding, and neither Ibis nor Isis has received any notices regarding any of the foregoing. No loss or expiration of any material Business IP is pending or reasonably foreseeable or, to Isis' or Ibis' Knowledge, threatened, except for patents expiring at the end of their statutory terms (and not as a result of any act or omission by either Ibis or Isis, including, without limitation, a failure to pay any required maintenance fees) or limitations to the scope of claims of any pending patent application made during the ordinary course of prosecuting such pending patent applications. Complete copies of all file histories for issued patents and pending patent applications of the Business IP owned or held by either Ibis or Isis have been provided to AMI.

(vii) To Isis' or Ibis' Knowledge, (A) no Person has infringed (directly, contributorily, by inducement or otherwise), or misappropriated any of the Business IP and (B) no Person is infringing (directly, contributorily, by inducement or otherwise) or misappropriating any of the Business IP.

(viii) Ibis has sufficient right, title and interest in and to the Business IP: (A) to conduct the Business, including the development, manufacture and commercialization of the T5000 Biosensor System (including the [***]) and the assay kits specifically listed in the [***] on a worldwide basis, with no payment obligation to any Person, except pursuant to an IP Contract, and (B) to make, have made, import, use, offer for sale, or sell any product (including [***]) currently marketed by the Business and the assay kits specifically listed in the [***] [***] without infringing (directly, contributorily, by inducement or otherwise), misappropriating or conflicting with any Intellectual Property rights of any Person. The Business IP is and will be as of the Closing Date, owned by or available for use by Ibis on terms and conditions identical to those under which it was owned or used by Ibis and the Business prior to the date hereof.

(ix) To Isis' or Ibis' Knowledge, Ibis has sufficient right, title and interest in and to the Business IP: (A) to develop, manufacture and commercialize the [***] on a worldwide basis, with no payment obligation to any Person, except pursuant to an IP Contract made available to AMI, and (B) to make, have made, import, use, offer for sale, or sell the [***] without infringing (directly, contributorily, by inducement or otherwise), misappropriating or conflicting with any Intellectual Property rights of any Person.

(x) No funding, facilities or resources of a Governmental Authority, university, college, other educational institution or research center or funding from third parties was used in the development of any of the Business IP and no Governmental Authority, university, college, other educational institution or research center has any claim or right in or to any of the Business IP.

(xi) Each current or former employee of each Isis Party or any of their respective Affiliates, who was involved in, or who contributed to, the creation or development of any Business IP, executed the standard form of proprietary rights agreement set forth in Schedule 5.1(l)(xi) upon commencement of his or her employment and each such current or former employee and any consultant or independent contractor who was involved in, or who contributed to, the creation or development of any Business IP has validly assigned all right, title and interest in and to such Business IP to Ibis.

(xii) None of the Transaction Documents nor the transactions contemplated by any of the Transaction Documents would result in or reasonably be expected to result in: (A) Ibis, AMI or any of their respective Affiliates granting to any Person any right to or with respect to any Intellectual Property owned by, or licensed to, any of them as a result of any Encumbrance or Contract to which, Ibis or any of their Affiliates is a party or bound by, (B) other than standard non-solicitation agreements entered into in the ordinary course of business and made available to AMI, Ibis, AMI or any of their respective Affiliates being bound by, or subject to, any non-compete or other

material restriction on the operation or scope of their respective businesses as a result of any Encumbrance or Contract to which Isis, Ibis or any of their Affiliates is a party or bound by, (C) other than as contemplated by the Acquisition Agreement, Ibis, AMI or any of their respective Affiliates being obligated to pay any royalties or other material amounts, to increase or accelerate any royalty or payment obligation, or to offer any discounts, to any Person as a result of any Encumbrance or Contract to which Isis, Ibis or any of their Affiliates is a party or bound by, or (D) any adverse effect on Ibis' right, title or interest in and to any of the Business IP.

(xiii) All components of the current version of the T5000 Biosensor System perform in all material respects in accordance with their currently advertised, displayed, distributed or published specifications. All services that have been performed in the conduct of the Business were performed in material conformity with the terms and requirements of the related Contracts and all Applicable Laws. All Software included in the Business IP is free of any disabling codes or instructions, timer, copy protection device, clock, counter or other limiting design or routing and any "back door," "time bomb," "Trojan horse," "worm," "drop dead device," "virus" or other similar disabling codes, Software

routines or hardware components. No open source, public source or other Software that is licensed pursuant to a license that purports to require the distribution of, or access to, source code or purports to restrict one's ability to charge for distribution of Software (including, without limitation, any version of any Software licensed pursuant to any GNU general public license or limited general public license or other Software), was used in, incorporated into, integrated or bundled with any Software that has been used in the T5000 Biosensor System or any other product that has been distributed or is currently distributed. Ibis does not have any plans to include any such Software in any such system or Product. The source code for all Software included in the Business IP is sufficiently documented such that a software programmer of ordinary skill would be able to maintain and modify such source code using reasonable efforts.

(xiv) Without limiting any other representation or warranty herein, the computer and other information technology systems and networks owned or contracted for by Ibis have been maintained in accordance with normal industry practice, are in good operating condition and repair (except for ordinary wear and tear) and are sufficient for the operation of the Business. Each of Ibis and Isis has taken all reasonably necessary action to safeguard the computer and other information technology systems and networks used in the operation of the Business and there has been no unauthorized intrusions or breaches of the security of the computer and other information technology systems and networks used in the Business that have materially compromised or are currently materially compromising the security, integrity or operations of such systems or networks.

(xv) The individuals identified as the outside counsel involved in the development or prosecution of the Business IP on Schedule 1Section 1(qq) represent the outside counsel who have provided Isis or Ibis strategic legal and Intellectual Property advice related to the Business IP and the Ibis Business during the three (3) years prior to the Closing Date.

(m) Compliance with Other Instruments. Neither Ibis nor, with respect to the Business, Isis is in violation or default of any term of its charter documents, each as amended, or of any provision of any Contract to which it is party or by which the Business is bound or of any judgment, decree, order or writ.

(n) Litigation. There is no Claim pending or, to Isis' or Ibis' Knowledge, threatened against Ibis or, with respect to the Business, Isis (or against any Ibis or Isis employee (in their capacity as such)), at Law or in equity, or before or by any Governmental Authority, and to Isis' or Ibis' Knowledge, there is no reasonable basis for any of the foregoing. Neither Ibis nor, with respect to the Business, Isis is subject to any outstanding order, judgment, or decree issued by any Governmental Authority or any arbitrator. Neither Ibis nor any of its Affiliates has received any opinion or memorandum or advice from legal counsel to the effect that Ibis or the Business is or was exposed, from a legal standpoint, to any material liability.

(o) Tax Matters.

(i) **[**Ibis has not been required to file any Tax Returns.**]** All Taxes owed and due by Ibis have been paid. No claim has ever been made by an authority in any jurisdiction that Ibis is or may be subject to taxation by that jurisdiction. There are no Encumbrances on any of the assets used by Ibis that arose in connection with any failure (or alleged failure) to pay any Tax. Schedule 5.1(o)(i) contains a list of states, territories and jurisdictions (whether foreign or domestic) in which Ibis is required to file Tax Returns.

(ii) Ibis has withheld and paid all Taxes required to have been withheld and paid in connection with amounts paid or owing by Ibis to any employee, independent contractor, creditor, stockholder, or other third party, and all Forms W-2 and 1099 required with respect thereto have been properly completed.

(iii) There is no dispute or claim concerning any Tax liability of Ibis either (A) claimed or raised by any Governmental Authority or (B) as to which Isis or Ibis has Knowledge.

(iv) Neither Ibis nor, with respect to the Business, Isis, has waived any statute of limitations in respect of Taxes or agreed to any extension of time with respect to a Tax assessment or deficiency.

(v) To Isis' or Ibis' Knowledge based in good faith on advice of Deloitte & Touche LLP, (A) Ibis and Isis are and will be members of the same consolidated group, as such term is defined by Treasury Regulation § 1.1502-1(h), with Isis being the common parent of such consolidated group for all taxable years through and including the Closing and (B) unless the provisions of the Code pertaining to filing Tax Returns as a consolidated group are amended prior to the Closing, Ibis and Isis will be eligible to file a consolidated Tax Return in lieu of separate Tax Returns with respect to income Tax imposed by Chapter 1 of the Code for all taxable years through and including the Closing.

(vi) Ibis is not and will not at the Closing be a party to any oral or written Tax sharing agreements or arrangements.

(p) Employees.

(i) Neither Ibis nor, with respect to the Business, Isis, is party to any collective bargaining agreement. There is no labor union organizing activity pending or, to Isis' or Ibis' Knowledge, threatened with respect to Ibis. Each of Ibis and, with respect to the Business, Isis has complied with all applicable Laws relating to the employment of labor and, within the last five (5) years, neither Ibis nor Isis, with respect to the Business, has experienced any strike, work stoppage, lockout, grievance, unfair labor practice claim or other labor relation problem, including, without limitation, any written dispute with or Claim by former employees regarding termination and/or severance pay. To the Knowledge of Isis or Ibis, no executive, key employee or group of employees of Ibis has any plans to terminate employment with Ibis. In the past three (3) years, Ibis and Isis have complied in all respects with the notification provisions (or paid severance in lieu thereof) of the WARN Act and applicable similar state or local laws. No executive, key employee or group of employees of Ibis or the Business has been terminated or resigned their employment since the Investment Date.

(ii) Schedule 5.1(p)(ii) contains a true and complete list of each employment (other than at-will offer letters with no severance, compensation term guarantee or material benefit), bonus, fringe benefit, deferred compensation, incentive compensation, stock purchase, stock option, stock appreciation right or other stock-based incentive, severance, change-in-control, or other termination pay, hospitalization or other medical, disability, life or other insurance, supplemental unemployment benefits, profit-sharing, pension, or retirement plan, program or Contract and each other employee benefit plan, program or Contract sponsored, maintained or contributed to or required to be contributed to by Ibis, or by any trade or business, whether or not incorporated (an "ERISA Affiliate"), that together with Ibis or Isis would be deemed a "single employer" under Section 414(b), (c), (m) or (o) of the Code, for the benefit of any current or former employee or director of Ibis (the "Plans"). Schedule 5.1(p)(ii) identifies each Plan that is an "employee welfare benefit plan" or "employee pension benefit plan" as such terms are defined in Sections 3(1) and 3(2) of ERISA (such plans being hereinafter referred to collectively as the "ERISA Plans").

(iii) Neither Ibis nor Isis has any formal plan or binding commitment to create any additional Plan or modify or change any existing Plan that would affect any current or former employee or director of Ibis, except as required by Applicable Law or to conform such Plan to the requirements of any Applicable Law. Except for the Master Agreement and this Agreement, there are no Contracts or omissions that would prevent or impair any Plan (including any Plan covering retirees or other former employees) from being amended or terminated by Ibis or Isis prior to or at the Closing, or, with respect to the Plans listed on Schedule 5.1(p)(xii) if any, by Ibis or AMI (or any successor thereto) on or at any time after the Closing.

(iv) Neither Isis nor Ibis has incurred and has no reason to expect that either will incur any liability to the Pension Benefit Guaranty Corporation (other than premium payments) or otherwise under Title IV of ERISA (including any withdrawal liability) or under the Code or any Applicable Law with respect to any employee pension benefit plan that Isis or Ibis, or any other entity that together with Isis or Ibis is treated as a single employer under Section 414 of the Code, maintains or ever has maintained or to which it contributes, ever has contributed, or ever has been required to contribute.

(v) Neither Ibis nor Isis, nor any of the ERISA Plans, nor any trust created thereunder, nor to Isis' or Ibis' Knowledge, any trustee or administrator thereof has engaged in a transaction or has taken or failed to take any action in connection with which Ibis could be subject to any material liability for either a civil penalty assessed pursuant to Sections 409 or 502(i) of ERISA or a tax imposed pursuant to Sections 4975, 4976 or 4980B of the Code.

(vi) Each Plan is in all material respects in compliance, and has been administered in all material respects in accordance, with the applicable provisions of ERISA, the Code and all other Applicable Laws, including, but not limited to, medical continuation under Section 4980B of the Code. Neither Isis nor Ibis has (A) engaged in any transaction prohibited by ERISA or the Code; (B) breached any fiduciary duty owed by it with respect to the Plans; or (C) failed to file and distribute timely and properly all reports and information required to be filed or distributed in accordance with ERISA or the Code.

(vii) Other than routine claims for benefits, there are no Claims, Internal Revenue Service or Department of Labor compliance programs or other proceedings pending or, to Isis' or Ibis' Knowledge, threatened against or otherwise involving any Plan.

(viii) Each Plan which is intended to be qualified under Section 401(a) of the Code (A) has been amended to reflect all requirements under the Code which are required to be adopted prior to the end of the applicable remedial amendment period and (B) has received from the Internal Revenue Service a favorable determination letter which considers the terms of the Plan as amended for such changes in Law.

(ix) None of the Plans obligates Isis or Ibis either (A) to pay any separation, severance, termination or similar benefit to Ibis Employees or (B) to make an excess parachute payment within the meaning of Code Section 280G.

(x) No Plan provides benefits, including without limitation death or medical benefits (whether or not insured), with respect to current or former employees of Ibis after retirement or other termination of service (other than (A) coverage mandated by any Applicable Law, (B) death benefits or retirement benefits under any employee pension benefit plan or (C) benefits, the full direct cost of which are borne by the current or former employee (or beneficiary thereof)).

(xi) To Isis' or Ibis' Knowledge, other than as provided under the terms of the Plans, neither Ibis nor Isis has made any representation or commitment to, or entered into any formal or informal understanding with, any Ibis employee with respect to compensation, benefits, or terms of employment to be provided by AMI or Ibis or any of their respective Affiliates at or subsequent to the Closing.

(xii) Except for the Permitted Employee Compensation Plan, Ibis neither sponsors nor maintains nor has any liability for (A) any of the Plans or (B) any other employee benefit plans or arrangements.

(xiii) All contributions, premiums or payments under or with respect to each Plan which are or were due have been paid.

(q) Compliance with Laws; Licenses.

(i) Ibis, the Business and, with respect to the Business, Isis are not in material violation of any Law. Ibis, the Business, and, with respect to the Business, Isis and Ibis' and Isis' Representatives have complied with, and are in material compliance with, all Applicable Laws, including, without limitation, the federal Food, Drug, and Cosmetic Act, as amended and regulations promulgated thereunder, and all U.S. Food and Drug Administration ("FDA") or its foreign equivalent regulations governing, among other things, the protection of human subjects and regulations governing clinical investigators. No governmental orders, permissions, consents, approvals or authorizations are required to be obtained and no registrations or declarations are required to be filed in connection with the execution and delivery of the Transaction Documents or the Transfer of the Remaining Shares.

(ii) Ibis holds all Licenses necessary for the operation or conduct of the Business (including pursuant to Environmental Laws). Schedule 5.1(q)(ii) sets forth a list of all Licenses material to the Business (the "Material Licenses"). Ibis is and has been in compliance with all terms and conditions of such Material Licenses and all Material Licenses may be relied upon by Ibis immediately following the Closing for the lawful operation of the Business as conducted on and prior to the date hereof. Each Material License is valid, binding and in full force and effect and Ibis and the Business have complied in all material respects with all requirements of and are not in default under any Material License and have not received written or, to Isis' or Ibis' Knowledge, oral notice that the Business or Ibis is in violation of any of the terms or conditions of such Material License. No loss or suspension of any License nor any proceeding or investigation which is seeking such a loss or suspension is pending or, to Isis' or Ibis' Knowledge, threatened. Neither Ibis nor Isis is operating under any written or oral formal or informal agreement or understanding with any licensing authority, Regulatory Authority or any other Governmental Authority which restricts the conduct of the Business or requires Ibis or, with respect to the Business, Isis, to take or refrain from taking any actions.

(r) Environment, Health and Safety. Ibis and the Business have at all times materially complied with and are in material compliance with all Environmental Laws,

including, without limitation, all Licenses and other authorizations that are required pursuant to Environmental Laws for the ownership and occupation of the assets used by Ibis and the operation of the Business. Neither Ibis nor Isis, with respect to the Business is aware of or has reason to be aware of or has received any notice, request for information, report, order, directive, communication or other information, written or oral, regarding any actual or alleged violation of Environmental Laws, or any Claims or other liabilities or potential liabilities (whether accrued, absolute, contingent, unliquidated or otherwise) arising under Environmental Laws, relating to the Business, the Real Property or Ibis, which has not been resolved without liability to Ibis. Neither Ibis nor its Affiliates nor any of its legal predecessors has, in violation of Environmental Laws, treated, stored, disposed of, arranged for or permitted the disposal of, transported, handled, or Released, or exposed any Person to, any Hazardous Materials, or owned or operated any property or facility (and no such property or facility including the Real Property is contaminated by any such Hazardous Materials) so as to give rise to any current or future liability under Environmental Laws, including without limitation, any liability to investigate, remediate, cleanup, monitor or take any similar actions with respect to the environmental condition of any property (whether owned or non-owned), facility or treatment, storage or disposal facility. None of the following exists or to Isis' or Ibis' Knowledge, has ever existed at the Real Property: underground storage tanks, septic tanks, asbestos containing materials, polychlorinated biphenyls, lead-based paint, urea-formaldehyde, dumps, landfills, or waste disposal areas, sumps, pits, lagoons, surface impoundments or wetlands, or any contamination of any kind of the surface, subsurface, groundwater or surface water. Ibis has not assumed or become subject to, whether expressly or by operation of Law, any liabilities of any other Person arising under Environmental Laws or pursuant to any type of agreement. The consummation of the transactions contemplated by this Agreement do not impose any obligation on the Business under any Environmental Law or require notification to or consent of any Governmental Authority or third party pursuant to any Environmental Law. Ibis has provided to AMI copies of all material environmental Licenses, reports, audits, assessments, and investigations, and any other material environmental documents, relating to Ibis or the Business to the extent the foregoing are in the possession, custody, or control of Isis or any of its Affiliates or Ibis.

(s) Offering Valid. Assuming the accuracy of the representations and warranties of AMI contained in Section 5.2 hereof, the offer and sale of the Remaining Shares will be exempt from the registration requirements of the Securities Act, and will have been registered or qualified (or are exempt from registration and qualification) under the registration, permit or qualification requirements of all applicable state securities Laws. Neither Isis nor any agent on its behalf has solicited or will solicit any offers to sell or has offered to sell or will offer to sell all or any part of the Remaining Shares to any Person or Persons so as to bring the sale of such Remaining Shares by Isis within the registration provisions of the Securities Act or any state securities Laws.

(t) Financial Statements. Schedule 5.1(t) attached hereto contains the following financial statements (collectively the "Financial Statements"): (i) the profit and loss statement for the Division for the fiscal year ended December 31, 2007 and (ii) the profit and loss statement for Ibis and the related balance sheet (the "Most Recent Balance Sheet") for the **[ ]** month period ended **[ ]**. The Financial Statements have been prepared in accordance with GAAP throughout the periods covered thereby, present fairly in all material respects the financial condition of Ibis or the Division (as the case may be) as of such dates and

the results of operations of Ibis or the Division (as the case may be) for such periods, and are materially correct and complete and consistent with the books and records of Ibis (which books and records are materially correct and complete).

(u) Subsequent Events. Since the date of the Most Recent Balance Sheet, there has not been any material adverse change in the business, assets, liabilities, condition (financial or otherwise), operations, operating results, prospects, customer relations or supplier relations of Ibis and Ibis has and Isis has caused Ibis to conduct the Business in the ordinary course. Since the date of the Most Recent Balance Sheet:

(i) Ibis has not sold, leased, transferred, or assigned any of its assets to a third party, tangible or intangible, other than inventory in the ordinary course of business;

(ii) No party (including Ibis or Isis) has accelerated, terminated, modified, or canceled any material Contract (or series of related Contracts) to which Ibis is or was a party or by which the Business is or was bound;

(iii) Ibis has made capital expenditures consistent with its normal course of operations;

(iv) Ibis has not experienced any damage, destruction, or loss (whether or not covered by insurance) to its property over $50,000 in the aggregate;

(v) Ibis has not granted any increase in the base compensation of any employee, except in the ordinary course of business (including as to amount) or any bonus to, any employee, other than in the ordinary course of business;

(vi) Ibis has not amended, modified, or terminated any Plan;

(vii) Ibis has not entered into any transaction with any of its directors, officers, employees or Affiliates, except for transactions with its employees in the ordinary course of business;

(viii) Neither Ibis nor Isis has licensed, sublicensed, allowed any Encumbrance to exist on, abandoned, or permitted to lapse any Business IP or, except in the ordinary course of business, disclosed any Confidential Information of Ibis or the Business to any Person (other than AMI and AMI's Representatives);

(ix) Ibis has not made a change in its accounting methods; and

(x) Ibis has not committed in any binding manner to any of the foregoing.

(v) Brokers' Fees. There are no brokerage commissions, finders' fees or similar compensation due in connection with the transactions contemplated by the Transaction Documents based on any arrangement or agreement made by or on behalf of Isis or Ibis. To the extent there are any brokerage commissions, finders' fees or similar compensation due in

connection with the transactions contemplated by the Transaction Documents to [***], Isis shall be solely liable for any and all such amounts.

(w) Leased Real Property.

(i) Ibis does not own any real property and the ownership of any real property is not necessary for the operation of the Business. Ibis does not lease, sublease, license or otherwise grant any Person the right to use any real property. Neither Isis nor any of its Affiliates leases, subleases, licenses or occupies any real property used or occupied by, or necessary for the operation or conduct of, the Business.

(ii) Schedule 5.1(w)(ii) sets forth the names of the lessor and lessee, the address of each parcel of real property used by Ibis (collectively, the "Leased Real Property"), and a list of all leases, subleases, licenses and other agreements (whether written or oral) (collectively, "Leases") for each such Leased Real Property. None of the Leases is a ground lease. Ibis and Isis have delivered to AMI a true and complete copy of each such Lease document, and in the case of any oral Lease, a written summary of the material terms of such Lease. Ibis does not own any structures, improvements or fixtures located on any Leased Real Property (collectively, "Leasehold Improvements") and no Leasehold Improvements other than those provided to Ibis under the Corporate Services Agreement are material to the operation of the Business.

(iii) Each such Lease is legal, valid, binding, enforceable and in full force and effect.

(iv) Neither Ibis nor, to Isis' or Ibis' Knowledge, any other party to a Lease is in breach or default under such Lease, no event has occurred or circumstance exists which, with the delivery of notice, the passage of time or both, could reasonably be expected to constitute such a breach or default, or permit the termination, modification or acceleration of rent under such Lease and neither Ibis nor Isis has received notice that the Leased Real Property is in violation of any Applicable Law.

(v) No security deposit or portion thereof deposited with respect to such Lease has been applied in respect of a breach or default under such Lease which has not been redeposited in full. Neither Ibis nor any other Person owes any brokerage commissions, finder's fees, free rent or allowances with respect to such Lease.

(x) Contracts.

(i) Schedule 5.1(x)(i) lists the following Contracts relating to the Business or to which Ibis is a party: (A) Contract for the employment of any officer, individual employee, or other Person on a full-time, part-time, consulting, or other basis or Contract relating to loans to officers, directors, employees or Affiliates; (B) agreement or indenture relating to borrowed money or other Indebtedness or the mortgaging, pledging, or otherwise placing an Encumbrance on assets or Capital Stock of Ibis; (C) lease or agreement under which Ibis is the lessee of or holds or operates any property, real or personal, owned by any other party, except for any lease or agreement for real or personal property under which the aggregate annual consideration is less than or equal to

$25,000; (D) lease or agreement under which Ibis is the lessor of or permits any Person to hold or operate any property, real or personal, owned or controlled by Ibis; (E) distribution or franchise agreement; (F) agreement with a term of more than six months and (1) which is not terminable by Ibis upon less than 90 days' notice without penalty or (2) which involves aggregate annual consideration in excess of $25,000; (G) agreements relating to ownership of or investments in any business or enterprise, including joint ventures and minority equity investments; (H) Contract prohibiting it from freely engaging in any business or competing anywhere in the world; (I) except as otherwise disclosed on Schedule 5.1(x)(i) any other Contract or group of related Contracts with the same party or group of affiliated parties that involves aggregate annual consideration from or to Ibis in excess of $100,000; or (J) any Contract that is otherwise material to Ibis and/or the Business, including, without limitation, any IP Contract or Government Contract, whether or not entered into in the ordinary course of business and whether or not performance thereunder has been completed. All of the Contracts and other similar arrangements set forth on or required to be set forth on Schedule 5.1(x)(i) (the "Ibis Contracts").

(ii) All of the Ibis Contracts are valid, binding, enforceable and in full force and effect, and the transactions contemplated by the Transaction Documents will not cause such Contracts to cease to be valid, binding, enforceable and in full force and effect on identical terms following the Closing. Each of Isis or Ibis, as applicable, and, to Isis' or Ibis' Knowledge, each counterparty thereto has performed all material obligations required to be performed by it and is not in default under or in breach of or in receipt of any claim of default or breach under any Ibis Contract. No event has occurred which with the passage of time or the giving of notice or both would result in a default, breach or event of noncompliance by either Ibis or Isis or, to Isis' or Ibis' Knowledge, any other party under any such Ibis Contract. Neither Isis nor Ibis has received

notice of the intention of any party to cancel or terminate any Ibis Contract and, to Isis' or Ibis' Knowledge, there has not been any breach or anticipated breach by the other parties to any such Ibis Contract.

(iii) Isis has provided AMI with a true and correct copy of all Ibis Contracts in each case together with all amendments, waivers, or other changes thereto (all of which are disclosed on Schedule 5.1(x)(i)). Schedule 5.1(x)(i) contains an accurate and complete description of all material terms of all oral Contracts referred to therein.

(y) Insurance. Schedule 5.1(y) attached hereto lists and briefly describes each insurance policy maintained by Ibis or Isis with respect to the Business (the "Insurance Policies"), together with a claims history for the past five (5) years for Ibis and, with respect to the Business, Isis. All of the Insurance Policies are in full force and effect, and neither Ibis nor Isis with respect to the Business is in default with respect to its obligations under any such insurance policy and neither Ibis nor Isis, with respect to the Business has been denied insurance coverage. Neither Ibis nor Isis, with respect to the Business has any self-insurance or co-insurance programs.

(z) Customers and Suppliers. Schedule 5.1(z) accurately sets forth a list of the Business' top ten customers by revenue for the fiscal year ended **[**December 31, 2007**]** and the **[ ]** month period ended **[ ]**. Except as set forth on Schedule 5.1(z), neither Isis nor Ibis has received any indication from any material customer of the Business or any Governmental Authority to the effect that, and neither Isis nor Ibis has any reason to believe that, such customer or Governmental Authority will in the future stop, or materially decrease the rate of buying products or services from the Business. Schedule 5.1(z) also accurately sets forth a list of the Business' top ten suppliers by dollar amount for the **[ ]** month period ended **[ ]**. Except as set forth on Schedule 5.1(z), neither Isis nor Ibis has received any indication from any material supplier of the Business to the effect that, and neither Isis nor Ibis has any reason to believe that, such supplier will stop or materially decrease the rate of providing products or services to the Business and its customers. Neither Isis nor Ibis is involved in any material dispute with any customer or supplier of or to the Business.

(aa) No Material Adverse Effect. Since September 30, 2007, there has been no Material Adverse Effect.

(bb) Names and Locations. During the five-year period prior to the date hereof, neither Ibis nor the Business has used any name or names under which it has invoiced account debtors or maintained records concerning the assets used in the operation of the Business, other than Ibis Biosciences, Inc. and all of the assets used in the operation of the Business are located at the Leased Real Property.

(cc) Directors, Officers and Bank Accounts. Schedule 5.1(cc) (i) sets forth a true and correct list of the directors and officers of Ibis and the title of each such officer. Schedule 5.1(cc) (ii) lists all of Ibis' bank accounts, safety deposit boxes and lock boxes (designating each authorized signatory with respect thereto).

(dd) Regulatory Filings. Ibis and Isis have made available for inspection by AMI all material registrations, filings or submissions made with any Regulatory Authority or the SEC, and reports of audits ever issued by any Governmental Authority made by or with respect to Ibis or the Business. Ibis or Isis has timely filed, or caused to be timely filed, all material reports, statements, documents, registrations, filings or submissions required to be filed by Ibis or the Business with any Governmental Authority in connection with the operation of Ibis or the Business. All such registrations, filings and submissions are in material compliance in all respects with all Laws when filed or as amended or supplemented, and no deficiencies have been asserted by any such Governmental Authority with respect to such registrations, filings or submissions.

(ee) Disclosure. Neither the Transaction Documents, nor any of the Schedules delivered in connection herewith or therewith, contains any untrue statement of a material fact or omits a material fact necessary to make the statements contained herein or therein, in light of the circumstances in which they were made, not misleading. To Isis' or Ibis' Knowledge, there is no event, circumstance or other fact which Isis or Ibis has not disclosed to AMI in writing which has had or would reasonably be expected to have a Material Adverse Effect.

5.2 Representations And Warranties Of AMI. As a material inducement to Isis to enter into this Agreement, AMI hereby represents and warrants to Isis that, except as set forth in the corresponding Section of the Disclosure Schedules, the following representations and warranties are as of the date hereof, and will be as of the Closing Date, true and correct:

(a) Power and Authority. AMI has the power, authority and the legal right to enter into the Transaction Documents and to perform its obligations hereunder and thereunder, and it has taken all necessary action required to authorize the execution and delivery of each such agreement and the performance of its obligations hereunder and thereunder.

(b) Enforceability. Each of the Transaction Documents has been duly executed and delivered on behalf of AMI and constitutes its legal, valid and binding obligation and is enforceable against it in accordance with its terms subject to the effects of bankruptcy, insolvency or other Laws of general application affecting the enforcement of creditor rights.

(c) Governmental Authority; Consents. All necessary consents, approvals and authorizations of all Governmental Authorities and other parties required to be obtained by AMI in connection with the execution and delivery of the Transaction Documents and the performance of its obligations hereunder and thereunder have been obtained.

(d) No Conflicts. The execution and delivery of the Transaction Documents by AMI and the performance of its obligations hereunder and thereunder (i) do not conflict with or violate any requirement of Applicable Law or any provision of its certificate of incorporation or bylaws and (ii) do not require any notice, conflict with, violate, or breach or constitute a default or require any consent not already obtained or give rise to any termination or acceleration right under, any contractual obligation by which such Party is bound.

(e) Due Organization; Qualification. AMI is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, with full corporate power and authority to enter into the Transaction Documents and to perform its obligations hereunder and thereunder.

(f) Investment Representations. AMI understands that the Remaining Shares have not been registered under the Securities Act. AMI also understands that the Remaining Shares are being offered and sold pursuant to an exemption from registration contained in the Securities Act based in part upon AMI's representations contained in this Agreement. AMI hereby represents and warrants as follows:

(i) *AMI Bears Economic Risk.* AMI may be required to bear the economic risk of its investment in the Remaining Shares indefinitely unless the Remaining Shares are registered pursuant to the Securities Act, or an exemption from registration is available.

(ii) *Acquisition for Own Account.* AMI is acquiring the Remaining Shares for AMI's own account for investment only, and not with a view towards their distribution.

(iii) *Accredited Investor.* AMI represents that it is an accredited investor within the meaning of Regulation D under the Securities Act.

(iv) *Ibis Information.* Ibis and Isis have given AMI an opportunity to discuss Ibis' business, management and financial affairs with directors, officers and management of Ibis and AMI has had an opportunity to review Ibis' operations and facilities.

(v) *Rule 144.* AMI acknowledges and agrees that the Remaining Shares are "restricted securities" as defined in Rule 144 promulgated under the Securities Act as in effect from time to time and must be held indefinitely unless they are subsequently registered under the Securities Act or an exemption from such registration is available. AMI has been advised or is aware of the provisions of Rule 144, which permits limited resale of shares purchased in a private placement subject to the satisfaction of certain conditions, including, among other things: the availability of certain current public information about Ibis, the resale occurring following the required holding period under Rule 144 and the number of shares being sold during any three-month period not exceeding specified limitations.

(g) Legends. AMI understands and agrees that the certificates evidencing the Remaining Shares will bear legends relating to restrictions on Transfer under federal and state securities Laws and legends required under applicable state securities Laws.

Section 6. RESERVED.

Section 7. PRE-CLOSING COVENANTS. The Parties agree as follows with respect to the period between the execution of this Agreement and the Closing:

7.1 General. Each of the Parties shall use its commercially reasonable efforts to take all action and to do all things necessary in order to consummate and make effective the transactions contemplated by this Agreement.

7.2 Affirmative Covenants of Isis and Ibis. Except as otherwise contemplated by this Agreement, between the date hereof and the Closing, each of Isis, with respect to the Business, and Ibis shall:

(a) conduct the Business only in the ordinary course; use commercially reasonable efforts to carry on the Business in the same manner as currently conducted and to keep Ibis' business organization and properties intact, including its business operations, physical facilities, working conditions, executives and key employees and Ibis' and the Business' relationships with lessors, licensors, suppliers, customers, carriers, consultants, independent contractors and others having business relations with Ibis or the Business;

(b) keep in full force and effect Ibis' organizational existence and all of its and the Business' assets, Contracts, rights, franchises, and Business IP and use commercially reasonable efforts to cause Ibis' and the Business' current insurance (or reinsurance) policies not to be canceled or terminated or any of the coverage thereunder to lapse;

(c) maintain the Real Property and other assets of Ibis (including the Business IP) in good repair, order and condition (normal wear and tear excepted) consistent with current needs, replace in accordance with prudent practices inoperable, worn out or obsolete assets with assets of good quality consistent with prudent practices and current needs and, in the event of a casualty, loss or damage to any of such assets or properties before the Closing Date, either repair or replace such damaged property or use the proceeds of such insurance in such other manner as mutually agreed upon by Isis and AMI; and

(d) maintain the books, accounts, and records of Ibis consistent with past practice and make capital expenditures at levels consistent with the past practices of Ibis and the Business.

7.3 Negative Covenants of Isis. Except as expressly contemplated by this Agreement or as set forth on Schedule 7.3, between the date hereof and the Closing, Ibis shall not and, with respect to Ibis and the Business, Isis shall not and shall cause Ibis not to:

(a) amend or waive any provision of Ibis' Certificate of Incorporation;

(b) take any action that would reasonably be expected to adversely affect the rights, preferences or privileges of the Shares, the Additional Shares or the Remaining Shares;

(c) take any action by written stockholder consent of Ibis without at least 2 Business Days prior written notice to AMI;

(d) redeem, repurchase, pay or declare dividends or other distributions with respect to any Capital Stock of Ibis;

(e) issue any Capital Stock of Ibis or any rights to acquire Capital Stock of Ibis;

(f) authorize or designate, whether by reclassification or otherwise, any new class or series of Capital Stock of Ibis or any increase in the authorized or designated number of any such class or series of Capital Stock of Ibis;

(g) enter into any transaction of merger, consolidation or sale of control, or liquidate, reorganize, recapitalize, wind up or dissolve Ibis, or Transfer any portion of Ibis' Capital Stock, properties, assets or business other than transfers of inventory in the ordinary course of business;

(h) sell, transfer, assign, license or sublicense, or allow any Encumbrance on any Business IP other than (i) rights of the U.S. federal government in Intellectual Property pursuant to the Government Contracts set forth on Schedule 5.1(l)(iii) or new Government Contracts entered into in the ordinary course of business and (ii) end user license agreements related to the Software embodied in the T5000 Biosensor Systems that are issued in the ordinary course of business solely to purchasers of T5000 Biosensor Systems;

(i) abandon or permit to lapse any Business IP other than patents expiring at the end of their statutory terms (and not as a result of any act or omission by either Ibis or Isis, including, without limitation, a failure to pay any required maintenance fees) and limitations to the scope of claims of any pending patent application made during the ordinary course of prosecuting such pending patent applications;

(j) disclose any Confidential Information of the Business to any Person (other than AMI and its Representatives) other than in the ordinary course of business;

(k) create, incur, guarantee, assume, or be liable for any Indebtedness, other than Permitted Indebtedness in the ordinary course of business;

(l) subject any tangible asset of the Business to any Encumbrance, other than Permitted Encumbrances in the ordinary course of business and rights of the U.S. federal government in certain equipment purchased using government funds pursuant to (i) the Government Contracts set forth on Schedule 5.1(l)(iii) or (ii) new Government Contracts entered into in the ordinary course of business;

(m) (i) make any loan to or enter into any transaction with any officer, employee, partner or Affiliate, (ii) increase any officer's, employee's or partner's compensation outside the ordinary course of business, (iii) increase or accelerate any benefit, vesting schedule, obligation, subsidy or similar feature under any Plan outside the ordinary course of business, (iv) establish any Plan (except for the Permitted Employee Compensation Plan as contemplated by this Master Agreement), or (v) amend any Plan outside the ordinary course of business or commence making contributions to any multiemployer plan;

(n) make any acquisition, by means of merger, consolidation or otherwise, or any disposition, of assets or Capital Stock of any other Person;

(o) make any loans or capital contributions to, or investments in, any other Person, except advances to employees for reasonable expenses incurred in the ordinary course of business;

(p) enter into any Contract or amend any Contract required to be disclosed or to have been disclosed on Schedule 5.1(l) or Schedule 5.1(x), except in the ordinary course of business;

(q) enter into any strategic alliance, joint venture or joint marketing arrangement or agreement;

(r) delay or defer maintenance or repairs on any of Ibis' assets;

(s) waive or release any material Claim of Ibis;

(t) except as may be required by GAAP, make any material changes in policies or practices relating to selling practices, returns, discounts or other terms of the Business or accounting therefor, or in respect of the payment of trade payables or other similar liabilities incurred in connection with the operation of Ibis;

(u) increase or decrease marketing or promotional spending in any material respect from the rates established as of the date hereof, other than in the ordinary course of business;

(v) incur or guarantee any liability other than in connection with the performance or consummation of this Agreement;

(w) incur or commit to incur any capital expenditures in excess of $100,000 which would be payable after the Closing;

(x) take or omit to take any action that has or could reasonably be expected to have the effect of accelerating to pre-Closing periods sales that would otherwise be expected to occur after the Closing or otherwise in anticipation of the transactions contemplated hereby;

(y) take or omit to take any action that has or could reasonably be expected to have the effect of decelerating to post-Closing periods any payments or liabilities that would otherwise be expected to occur prior to the Closing or otherwise in anticipation of the transactions contemplated hereby;

(z) except as otherwise contemplated by this Agreement, pay, discharge, settle or satisfy any claim, liability or obligation or litigation (whether or not commenced prior to the date of this Agreement) outside the ordinary course of business;

(aa) take any other action which would reasonably be expected to interfere with, impede or materially delay the transactions contemplated hereby or dilute the benefits hereof to AMI and its Affiliates; or

(bb) commit, or enter into any agreement to do, any of the foregoing.

7.4 Notices and Consents. Each of the Parties will give any notices to, make any filings with and use its commercially reasonable efforts to obtain any authorizations, consents and approvals of third parties and Governmental Authorities in connection with the matters referred to in Sections 5.1(c) (Governmental Authority; Consents) and 5.1(d) (No Conflicts) above, including without limitation the transfers of Licenses.

7.5 Full Access. Ibis will cooperate with AMI in AMI's investigation of Ibis and the Business, and Ibis will permit AMI and its employees, agents, accountants, attorneys, environmental consultants, and other authorized representatives to (i) have full access to the premises, books and records of Ibis and, to the extent related to the Business, Isis, upon reasonable prior notice during normal business hours, (ii) visit and inspect any of the properties of Ibis and, to the extent related to the Business, Isis, upon reasonable prior notice during normal business hours and (iii) discuss the affairs, finances and accounts of Ibis with the officers, directors, employees, key customers, suppliers and independent accountants of Ibis.

7.6 Transition Assistance. From and after the date hereof, neither Isis nor Ibis will in any manner take or cause to be taken any action which is designed, intended or might reasonably be anticipated to have the effect of discouraging current or potential customers,

suppliers, licensors, lessors, independent contractors, consultants, employees and other associates of Ibis or the Business from establishing or maintaining the same business relationships with AMI after the date of this Agreement as were maintained with Ibis or the Business prior to the date of this Agreement.

7.7 Notice of Developments.

(a) Isis shall promptly (once Isis or Ibis obtains Knowledge thereof, but in any event within [***] of such Knowledge) inform AMI in writing of any inaccuracy in or breach of the representations and warranties contained in Section 5.1 or any breach of any covenant hereunder by Ibis or Isis. No such disclosure by Isis pursuant to this Section 7.7, however, shall be deemed to cure any breach of any representation or warranty or covenant contained herein for purposes of determining the fulfillment of the conditions set forth in Sections 4.1(a) and 4.1(b) as of the Closing or for purposes of determining the liability of Isis with respect thereto under Sections 8.2(a)(i), 8.2(a)(ii) or 8.2(a)(iv).

(b) AMI shall promptly (once AMI obtains Knowledge thereof, but in any event within three (3) Business Days of such Knowledge) inform Isis in writing of any inaccuracy in or breach of the representations and warranties contained in Section 5.2 or any breach of any covenant hereunder by AMI. No such disclosure by AMI pursuant to this Section 7.7, however, shall be deemed to cure any breach of any representation or warranty or covenant contained herein for purposes of determining the fulfillment of the conditions set forth in Sections4.2(a) and 4.2(b) as of the Closing or for purposes of determining the accuracy of the representations and warranties contained in Section 5.2 and the liability of AMI with respect thereto under Section 8.2(c).

7.8 Exclusivity.

(a) Until the Closing, neither Isis, nor Ibis nor any of their respective Affiliates shall (and each shall (i) cause its Representatives and (ii) instruct its investment bankers, attorneys and accountants, not to), directly or indirectly, encourage, solicit, approve or recommend or participate in or initiate discussions or negotiations with, or provide any information to, any Person or group (other than AMI and its Representatives) concerning any Purchase Offer.

(b) Isis shall promptly, but in any event within [***] [***], notify AMI of the existence of any attempted [***] by a non-intermediary principal received by Ibis or Isis or their respective Representatives, regarding any [***] and Ibis and Isis shall promptly, but in any event within [***] [***], communicate to [***] which they may receive (and will immediately provide to AMI [***] and the [***]. Isis and Ibis shall promptly provide to AMI any [***] provided to any other Person by or on behalf of Ibis or Isis in connection with [***].

7.9 Indebtedness and Intercompany Accounts.

(a) Prior to the Closing, Isis (i) shall assume, extinguish, repay or contribute as equity, or shall cause to be assumed, extinguished, repaid or contributed as equity, all Indebtedness and ancillary obligations thereto owed by Ibis to any Person (including Isis and its Affiliates) (not including the amount of any Indebtedness that is Permitted Indebtedness under

clauses (i) or (ii) of the Permitted Indebtedness definition that is owed to any Person other than Isis or any of its Affiliates), such that Ibis shall have no Indebtedness or ancillary obligations to any Person (not including the amount of any Indebtedness that is Permitted Indebtedness under clauses (i) or (ii) of the Permitted Indebtedness definition that is owed to any Person other than Isis or any of its Affiliates) and (ii) shall, and shall cause its Affiliates to, repay in full all Indebtedness and ancillary obligations thereto it or they owe to Ibis.

(b) Prior to the Closing, Isis shall, and shall cause its Affiliates to, settle or extinguish all intercompany receivables and payables that were incurred on or prior to the Closing and that arose from transactions between Isis or its Affiliates (other than Ibis), on the one hand, and Ibis, on the other hand.

(c) At the Closing, Isis shall cause to be delivered to AMI (i) the Remaining Shares free and clear of all Encumbrances, (ii) the assets of Ibis free and clear of all Encumbrances, other than Permitted Encumbrances and (iii) payoff letters with respect to any Indebtedness of Ibis to be paid by AMI at the Closing (in each case in form and substance reasonably satisfactory to AMI).

(d) At or prior to the Closing, Isis and Ibis shall terminate the Corporate Services Agreement and shall amend the Contribution Agreement as reasonably requested by AMI.

7.10 Distribution of Cash and Grants Receivable.

Immediately prior to the Closing, Ibis may distribute (i) all of its cash and cash equivalents and (ii) Grants Receivable to Isis.

Section 8. ADDITIONAL AGREEMENTS.

8.1 Survival. The covenants in this Agreement shall survive the Closing indefinitely, except as otherwise provided herein. The representations and warranties in this Agreement shall survive the Closing as follows:

(a) the Fundamental Isis Representations and Fundamental AMI Representations shall terminate on [***];

(b) the representations and warranties in Section 5.1(o) (Tax Matters), Section 5.1(p) (Employees) and Section 5.1(r) (Environment, Health and Safety) shall terminate [***] and the representations and warranties in Section 5.1(l) (Intellectual Property) shall terminate on the [***] anniversary of the Closing Date; and

(c) all other representations and warranties in this Agreement shall terminate on the [***] anniversary of the Closing Date.

Notwithstanding the foregoing, claims for indemnification pursuant to Section 8.2 as to which the Indemnified Party has given the Indemnifying Party proper notice pursuant to Section 10.6 prior to the expiration of the applicable survival period shall survive such expiration

until such claims are resolved by written agreement of the Parties or by order of a court of competent jurisdiction.

8.2 Indemnification.

(a) Isis shall indemnify, defend and hold harmless AMI, Ibis, their respective officers, directors, shareholders, employees, representatives, agents and Affiliates (collectively, the "AMI Group") against any Losses which any of them may suffer, sustain, or become subject to, as a result of:

(i) the breach of any representation or warranty made by either Isis or Ibis in the Transaction Documents or in any certificate delivered by Isis or Ibis pursuant hereto or thereto;

(ii) the breach of any covenant or agreement made by either Isis or Ibis in the Transaction Documents or in any certificate delivered by Isis or Ibis pursuant hereto or thereto;

(iii) (A) any Plan of any entity that together with Ibis constitutes a controlled group of entities with Isis under Section 414(b), (c), (m) or (o) of the Code, (B) any former employee of Ibis or Isis who is not an Ibis Employee (regardless of when such Loss arises) and (C) any Ibis Employees, in each case, incurred on or prior to the Closing Date; and

(iv) the conduct or operation of the Business or ownership or occupancy of the assets used in the Business on or prior to the Closing Date.

(b) With respect to claims for indemnification pursuant to Sections 8.2(a)(i), 8.2(a)(iii) or 8.2(a)(iv) above, Isis will be liable to the AMI Group for any such Losses only if the aggregate amount of all such Losses relating to all such breaches exceeds [***], in which case Isis will be [***]. Notwithstanding the foregoing, the recovery limitations set forth in this Section 8.2(b) shall not apply to any Losses suffered as a result of the breach by Isis or Ibis of any [***].

(c) AMI shall indemnify, defend and hold harmless Isis, its respective officers, directors, shareholders, employees and Affiliates (the "Seller Group") against any Losses which any of them may suffer, sustain or become subject to, as the result of:

(i) the breach of any representation or warranty made by AMI in the Transaction Documents or in any certificate delivered by AMI pursuant hereto or thereto;

(ii) the breach of any covenant or agreement made by AMI in the Transaction Documents or in any certificate delivered by AMI pursuant hereto or thereto; and

(iii) the conduct or operation of the Business or ownership or occupancy of the assets used in the Business after the Closing Date.

(d) With respect to claims for indemnification pursuant to Sections 8.2(c)(i) and 8.2(c)(iii) above, AMI will be liable to the Seller Group for any such Losses only if the aggregate amount of all such Losses relating to all such breaches exceeds [***], in which case AMI will be [***]. Notwithstanding the foregoing, the recovery limitations set forth in this Section 8.2(d) shall not apply to any Losses suffered as a result of the breach by AMI of any [***].

(e) If any third party shall notify any Party to this Agreement (the "Indemnified Party") of any matter which may give rise to a claim (a "Third Party Claim") for indemnification against any other Party to this Agreement (the "Indemnifying Party") under this Section 8.2, then the

Indemnified Party shall notify the Indemnifying Party thereof; provided that the failure to so notify the Indemnifying Party shall not relieve the Indemnifying Party of its obligations hereunder except to the extent such failure shall have actually materially prejudiced the Indemnifying Party. Once the Indemnified Party has given notice of the matter to the Indemnifying Party, the Indemnified Party shall defend against the matter in any manner it reasonably may deem appropriate. The Indemnifying Party may, at its sole cost and expense, participate in the defense of such Claim with co-counsel of its choice. Notwithstanding anything herein to the contrary, the Indemnifying Party shall not have the right to participate in such defense if the claim in which the Indemnifying Party seeks to participate (i) seeks non-monetary relief that does not seek to obtain a license or other access to, restrict the scope of, or adversely affect the enforceability of, any Intellectual Property controlled by the Indemnifying Party, (ii) involves criminal allegations against an Indemnified Party or (iii) is one in which the Indemnifying Party is also a party and joint representation would be inappropriate or there may be legal defenses available to the Indemnified Party which are different from or additional to those available to the Indemnifying Party. The Indemnified Party will not consent to the entry of any judgment with respect to the matter or enter into any settlement with respect to the matter without the Indemnifying Party's prior written consent (not to be unreasonably withheld, conditioned or delayed).

(f) None of the AMI Group or the Seller Group shall be entitled to recover any Losses relating to any matter arising under one provision of this Agreement to the extent that any such Person has already recovered Losses with respect to such matter pursuant to other provisions of this Agreement (including but not limited to the earnout payment reductions provided under Sections 2.3(a) and 2.3(b)) or the Master Agreement, it being understood and agreed that application of the foregoing provision shall not preclude the AMI Group from recovering any Losses incurred by the AMI Group in connection with the operation of the Business or the exploitation of the Business IP that are not [***].

(g) In determining (i) whether any representation, warranty, covenant or agreement contained herein has been breached or (ii) the amount of any Loss with respect thereto, any materiality, Material Adverse Effect, or similar qualification contained therein shall be disregarded.

(h) Indemnification for each Loss for which an Indemnifying Party, but for this Section 8.2(h), would be liable under Section 8.2(a) or Section 8.2(c) shall be reduced by the amount of any insurance proceeds actually paid to any member of the AMI Group or the Seller Group, as the case may be, by any unaffiliated third party with respect to such Loss, in

each case net of any Losses incurred by any member of the AMI Group or the Seller Group as the case may be in collecting such proceeds or payments; *provided* that this Section 8.2(h) shall not limit in any respect the right of any member of the AMI Group or the Seller Group, as the case may be, to pursue indemnification from an Indemnifying Party hereunder or from recovering for any Loss not reduced to zero pursuant to this Section 8.2(h). Nothing contained herein shall be deemed to cause any amounts for which a member of the AMI Group or the Seller Group, as the case may be, would ultimately be responsible, as a result of deductibles, self-insurance, indemnification of insurers, caps or similar items or arrangements, to not be subject to indemnification as "Losses" hereunder..

(i) For Tax purposes, the parties agree to treat all payments made under this Section 8.2 as adjustments to the Purchase Price.

8.3 Press Release and Announcements. On the date hereof, the Parties may issue a press release announcing **[**the execution of this Agreement//consummation of the transactions contemplated hereby**](3)** substantially in the form attached hereto as Exhibit E. Each Party agrees not to issue any other press release or other public statement relating to or make any public filing with respect to the Transaction Documents or the transactions contemplated hereby without the prior written consent of the other Party, which consent will not be unreasonably withheld or delayed. Each Party agrees to provide to the other Party a copy of any public announcement or public filing regarding the Transaction Documents or the subject matter thereof as far in advance as practicable under the circumstances prior to its scheduled release. Except under extraordinary circumstances, each Party will provide the other with an advance copy of any such announcement at least [***] prior to its scheduled release. The contents of any announcement or filing or similar publicity which has been reviewed, approved and released by the reviewing Party may be re-released by either Party without a requirement for advance notice or re-approval.

8.4 Expenses. Except as otherwise provided herein, each of AMI and Isis will bear its own costs and expenses (including, without limitation, all legal, accounting, consulting, investment banking, brokerage and other fees and expenses) incurred in connection with this Agreement and the transactions contemplated hereby; *provided* that all costs and expenses associated with obtaining third party consents with respect to Ibis Contracts or any Restricted Asset less than or equal to $[***] in the aggregate shall be borne by AMI and that, in accordance with Section 2.4, all such costs and expenses in excess of $[***] in the aggregate shall be borne by Isis; *provided* further, that the initial premerger notification and filing fee for HSR shall be borne by AMI, but any fees arising from any subsequent filings with respect thereto shall be borne equally by AMI and Isis.

8.5 Setoff. AMI and Ibis shall have the right to set off any claim AMI or Ibis may have against Isis under this Agreement or the Transition Services Agreement against any amounts owing to Isis under this Agreement; *provided* that (i) AMI provides written notice to

(3) Timing of press release TBD.

Isis of such setoff claim and (ii) initiates the ADR process described in Exhibit C hereto. AMI shall setoff any amounts pursuant to the foregoing by [***].

8.6 Certain Tax Matters.

(a) Transfer Taxes. All transfer, sales, use, stamp, registration and such Taxes and fees (including any penalties, interest and filing expenses) incurred in connection with this Agreement shall be paid by Isis, and Isis will prepare and file all necessary Tax Returns and other documentation with respect to all such transfer, documentary, sales, use, stamp, registration and other taxes and fees, and, if required by applicable law, the Parties will, and will cause their Affiliates to, cooperate in the execution of such Tax Returns. If AMI or one of its Affiliates is required to execute any Tax Return prepared by Isis under this section, Isis will provide a copy of such Tax Return to AMI at least 10 days prior to the anticipated filing of such Tax Return and AMI or its Affiliate shall execute the Tax Return, subject to Abbott's reasonable approval.

(b) Ad Valorem Taxes. All real property Taxes, personal property Taxes, ad valorem obligations and similar Taxes imposed on a periodic basis, in each case levied on Ibis, other than transfer Taxes provided for in Section 8.6(a) above, for a taxable period which includes (but does not end on) the Closing Date shall be apportioned between Isis and AMI as of the Closing Date based on the number of days of such taxable period included in the Pre-Closing Tax period and the number of days of such taxable period included in the Post-Closing period. Isis shall be liable for the proportionate amount of such Taxes that is attributable to the Pre-Closing Tax period. Within 90 days after the Closing, Isis and AMI shall present a reimbursement to which each is entitled under this Section 8.6(b) together with such supporting evidence as is reasonably necessary to calculate the proration amount; provided, that if the final Tax amount due for a taxable period that includes the Closing Date is not determined within such period, a reimbursement shall be based on the amount of the relevant Tax for the preceding taxable year, subject to an adjustment within 30 days after the final amount of such Tax is determined. The proration amount shall be paid by the Party owing it to the other within 10 days after delivery of such statement. Thereafter, Isis shall notify AMI upon receipt of any bill for real or personal property Taxes relating to Ibis, part or all of which are attributable to the Post-Closing Tax period, and shall promptly deliver such bill to AMI who shall pay the same to the appropriate taxing authority, provided that if such bill covers any portion of the Pre-Closing Tax period, Isis shall also remit prior to the due date of assessment to AMI payment for the proportionate amount of such bill that is attributable to the Pre-Closing Tax period. In the event that either Isis or AMI shall thereafter make a payment for which it is entitled to reimbursement under this Section 8.6(b), the other Party shall make such reimbursement promptly but in no event later than 30 days after the presentation of a statement setting forth the amount of reimbursement to which the presenting Party is entitled along with such supporting evidence as is reasonably necessary to calculate the amount of reimbursement. Any payment required under this Section 8.6(b) and not made within 10 days of delivery of the statement shall bear interest at the Applicable Rate for each day until paid.

(c) Tax Liability.

(i) Isis shall, in accordance with Section 8.2(a) (except as explicitly provided in this Section 8.6), indemnify and hold harmless the AMI Group

from any and all Losses arising from: (1) all Taxes (or the non-payment thereof) of Ibis for the Pre-Closing Tax Period, (2) all Taxes of any member of an affiliated, consolidated, combined or unitary group of which Ibis (or any predecessor thereof) is or was a member on or prior to the Closing Date, including pursuant to U.S. Treasury Regulation §1.1502-6 or any analogous or similar state, local, or foreign Law, and (3) any and all Taxes of any Person (other than Ibis) imposed on Ibis as a transferee or successor, by contract or pursuant to any Law, which Taxes relate to an event or transaction occurring before the Closing.

(ii) To the extent there is any taxable period that includes (but does not end on) the Closing Date (a "Straddle Period"), the amount of any Taxes based on or measured by income or receipts of Ibis for the Pre-Closing Tax Period shall be determined based on an interim closing of the books as of the close of business on the Closing Date (and for such purpose, the taxable period of any partnership or other pass-through entity in which Ibis holds a beneficial interest shall be deemed to terminate at such time) and the amount of other Taxes of Ibis for a Straddle Period that relates to the Pre-Closing Tax Period shall be deemed to be the amount of such Tax for the entire taxable period multiplied by a fraction the numerator of which is the number of days in the taxable period ending on the Closing Date and the denominator of which is the number of days in such Straddle Period.

(iii) AMI shall, in accordance with Section 8.2(c) (except as explicitly provided in this Section 8.6), indemnify and hold harmless the Seller Group from any and all Losses arising from: (1) all Taxes (or the non-payment thereof) of Ibis for the Post-Closing Tax Period, (2) all Taxes of any member of an affiliated, consolidated, combined or unitary group of which Ibis (or any successor thereto) is a member after the Closing Date, including pursuant to U.S. Treasury Regulation §1.1502-6 or any analogous or similar state, local, or foreign Law, and (3) any and all Taxes of any Person (other than Ibis) imposed on Ibis as a transferee or successor, by contract or pursuant to any Law, which Taxes relate to an event or transaction occurring after the Closing.

(iv) Isis' and AMI's obligations to indemnify for any Taxes under this Section 8.6 shall survive the Closing hereunder and continue until 30 days following the expiration of the statute of limitations on assessment of the relevant Tax. Notwithstanding the foregoing, any claim for indemnification shall survive such termination date if the Indemnified Party, prior to such termination date, shall have advised the Indemnifying Party in writing of facts that constitute or may give rise to an alleged claim for indemnification under this Section 8.6.

(d) Tax Returns.

(i) Isis shall file or cause to be filed when due (taking into account any extensions received from the relevant Tax authorities) (1) all Tax Returns that are required to be filed with respect to Ibis on or before the Closing Date, and (2) all Tax Returns that are required to be filed after the Closing Date with respect to income Taxes of Ibis with respect to all Pre-Closing Tax Periods, and shall pay when due (X) any

income Taxes due in respect of such Tax Returns, and (Y) any other Taxes due in respect of such Tax Returns that are due on or before the Closing Date.

(e) Contest Provisions.

(i) Isis shall have the sole right to control the conduct and resolution of any audit, litigation, contest, dispute, negotiation, or other proceeding with any Tax authority that relates to income Taxes of Ibis relating to a Pre-Closing Tax Period, including, without limitation, by selecting counsel of its choice to represent Ibis, unless Isis fails to assert such control within 30 days of receiving notice of such proceeding (each such proceeding for which Isis asserts such control, an "Isis Proceeding"); provided, that (1) Isis shall consult with AMI and keep AMI informed regarding the progress and any potential compromise or settlement of each Isis Proceeding; and (2) AMI shall be entitled to participate at its own expense in each Isis Proceeding and (C) Isis shall not settle or otherwise compromise any Isis Proceeding without the consent

of AMI to the extent such settlement or compromise would have an adverse effect on AMI or Ibis with respect to a Post-Closing Tax Period, which consent shall not be unreasonably withheld, conditioned or delayed.

(ii) AMI shall have the sole right to control the conduct and resolution of any audit, litigation, contest, dispute, negotiation, or other proceeding with any Tax authority relating to Taxes of Ibis that is not an Isis Proceeding, including, without limitation, by selecting counsel of its choice to represent Ibis (each such proceeding, an "AMI Proceeding"); provided, however, that (A) AMI shall consult with Isis regarding the progress and any potential compromise or settlement of any Isis Proceeding that relates to Taxes for which Isis may be liable pursuant to Section 8.6(c)(i) of this Agreement (an "Applicable AMI Proceeding"); (B) Isis shall be entitled to participate at its own expense in any Applicable AMI Proceeding; and (C) AMI shall not settle or otherwise compromise any Applicable AMI Proceeding without the consent of Isis to the extent such settlement or compromise would have an adverse effect on Isis or Ibis with respect to a Pre-Closing Tax Period, which consent shall not be unreasonably withheld, conditioned or delayed.

(iii) Provided AMI fails to assert control over an Applicable AMI Proceeding within 30 days of receiving notice of such proceeding, Isis shall have the sole right to control the conduct and resolution of an Applicable AMI Proceeding with any Tax authority, including, without limitation, by selecting counsel of its choice to represent Ibis; provided, however, that (1) Isis shall promptly consult with AMI regarding the progress and any potential compromise or settlement of any Applicable AMI Proceeding; (2) AMI shall be entitled to participate at its own expense in any Applicable Isis Proceeding; and (3) neither Isis nor Ibis shall settle or compromise any Applicable AMI Proceeding without the prior written consent of AMI, which shall not be unreasonably withheld, conditioned or delayed.

(f) Assistance and Cooperation. From and after the Closing Date, each of Isis and AMI shall:

(i) assist (and cause their respective Affiliates to assist) the other party in preparing any Tax Returns which such other party is responsible for preparing and filing in accordance with this Section 8.6;

(ii) cooperate fully in preparing for any audit, litigation, contest, dispute, negotiation, or other proceeding with any Tax authority regarding Taxes of Ibis;

(iii) make available to the other party and to any Tax authority, as reasonably requested, all information, records, and documents relating to Taxes or Tax Returns of Ibis (including, without limitation, information necessary to file extensions and make estimated Tax payments); and

(iv) furnish the other party with copies of all correspondence received from any Tax authority in connection with any applicable Isis Proceeding or AMI Proceeding.

(g) Code § 338(h)(10) Election. At AMI's option, Isis and AMI shall join in making an election under Code § 338(h)(10) (and any corresponding elections under state, local, or foreign tax law) (collectively a "§ 338(h)(10) Election") with respect to the purchase and sale of the Shares, **[**the Additional Shares**]** and the Remaining Shares, unless and to the extent the Code is amended to prevent or limit the filing of a § 338(h)(10) Election. Isis will pay any Tax attributable to the making of the § 338(h)(10) Election and will indemnify the AMI Group against any Losses arising out of any failure to pay such Tax.

(h) Allocation of Purchase Price. The Parties agree that the Purchase Price and the liabilities of Ibis (and other relevant items) will be allocated for tax purposes to the assets of Ibis in a manner consistent with Code §§ 338 and 1060 and the regulations thereunder. AMI, Ibis and Isis shall file all Tax Returns (including amended returns and claims for refund) and information reports in a manner consistent with such allocation.

8.7 Further Assurances. Isis will execute and deliver such further instruments of conveyance and transfer and take such additional action as AMI may reasonably request to effect, consummate, confirm or evidence the transfer to AMI of the Remaining Shares and the assets of the Business (including the Business IP and the Ibis Contracts), and Isis will execute such documents as may be necessary to assist AMI in preserving or perfecting its rights in the Shares, the Remaining Shares and the Business. Except for the services, funding and facilities provided under the Corporate Services Agreement, to the extent any assets used in the Business on or prior to the Closing Date (including the Business IP and the Ibis Contracts) or necessary to conduct the Business as conducted on and prior to the Closing Date (including the Business IP and the Ibis Contracts) or as contemplated to be conducted after the Closing Date have not been duly and fully transferred to Ibis as of such date, Isis hereby covenants, at its sole cost and expense and without further consideration by AMI, to take all such actions as may be requested by AMI to promptly transfer such assets to Ibis or AMI's designee.

8.8 Confidentiality.

(a) Each Party agrees that for a period of three (3) years after the Closing Date, a Party (the "Receiving Party") receiving or that has received Confidential Information of the other Party (the "Disclosing Party") will (i) maintain and cause its Representatives to maintain in confidence such Confidential Information using not less than the efforts such Receiving Party uses to maintain in confidence other proprietary information of similar kind and value (it being understood and agreed that AMI shall have no obligation to maintain the confidentiality of any Ibis Confidential Information and that Isis shall have an obligation to maintain the confidentiality of all Ibis Confidential Information pursuant to this Section 8.8), (ii) not disclose such Confidential Information except to the Receiving Party's employees or Affiliates having a need-to-know such Confidential Information solely for purposes of performing the Receiving Party's obligations under the Transaction Documents, (iii) not disclose such Confidential Information to any Person without the prior written consent of the Disclosing Party, except for disclosures expressly permitted by the Transaction Documents, and (iv) not use such Confidential Information for any purpose except those expressly permitted by the Transaction Documents. The provisions of this Section 8.8 shall supersede the provisions of Section 5.1, Section 5.2 and Section 5.3 of the Master Agreement which shall terminate and be of no further force or effect from and after the Closing Date. Upon AMI's request Isis will return or destroy (and certify to AMI any such destruction) all Confidential Information of AMI or its Affiliates and upon Isis' request, AMI will return or destroy (and certify to Isis any such destruction) all Confidential Information of Isis that is not Confidential Information of Ibis; *provided*, that AMI may retain one (1) copy of Isis' Confidential Information in Abbott's confidential files.

(b) To the extent (and only to the extent) that it is reasonably necessary, a Party may disclose Confidential Information belonging to the other Party in the following instances:

(i) when defending litigation related to the Confidential Information to be disclosed;

(ii) when complying with Applicable Laws (including, without limitation, the rules and regulations of the SEC or any national securities exchange, and compliance with Tax Laws) and with judicial process; and

(iii) disclosure, in connection with the performance of the Transaction Documents and solely on a need-to-know basis, to employees or independent contractors (including without limitation consultants and clinical investigators), each of whom prior to disclosure must be bound by written obligations of confidentiality and non-use no less restrictive than the obligations set forth in this Section 8.8; provided, that the Receiving Party will remain responsible for any failure by any Person who receives Confidential Information pursuant to this Section 8.8 to treat such Confidential Information as required under this Section 8.8.

(c) If and whenever any Confidential Information is disclosed in accordance with this Section 8.8, such disclosure will not cause any such information to cease to be Confidential Information except to the extent that such permitted disclosure results in a public disclosure of such information (other than by breach of this Agreement). Except as prohibited by

Law, the Receiving Party will notify the Disclosing Party of the Receiving Party's intent to make such disclosure pursuant to clauses (i) or (ii) of Section 8.8(b) sufficiently prior to making such disclosure so as to allow the Disclosing Party adequate time to take whatever action the Disclosing Party may deem appropriate to protect the confidentiality of the information. In addition, in the event any Party proposes to file with any Governmental Authority a Transaction Document, including, without limitation, as an exhibit to a registration statement, periodic report, or current report, the Party proposing to make such filing will notify the other Parties of such intention and will work in good faith with the other Parties to obtain confidential treatment of any material terms of the Transaction Documents that such other Parties request be kept confidential (except to the extent advised by counsel or such Governmental Authority that confidential treatment is not available for such information).

(d) At the Closing, Isis shall deliver to AMI all Confidential Information of the Business in Isis' or its Affiliates' possession and control and all copies thereof, in whatever form or medium, including, without limitation, written records, optical and magnetic media, and all other materials containing any such Confidential Information. If AMI requests, Isis shall promptly provide written confirmation that all such materials have been delivered to AMI.

(e) The existence and the terms and conditions of the Transaction Documents that the Parties have not specifically agreed to disclose pursuant to Section 8.8(b) or Section 8.3 will be considered Confidential Information of both Parties. AMI and, subject to the terms of Section 7.8, Isis may disclose such terms to a bona fide potential investor, investment banker, acquirer, merger partner or other potential business partner of AMI or Isis, respectively, and their attorneys and agents, *provided* that each such Person to whom such information is to be disclosed is informed of the confidential nature of such information and has entered into a written agreement with the Party requiring such Person to keep such information confidential.

8.9 Noncompetition and Nonsolicitation. The Parties hereby agree as follows:

(a) Noncompetition. During the period from the date hereof to and including the [***] anniversary of the Closing Date (the "Noncompete Period"), Isis and its Affiliates shall not engage in and shall not have any affiliation with any Person that engages in a line of business that competes with the Business as conducted on and prior to the Closing Date and as contemplated by Ibis and Isis to be conducted after the Closing Date, as reflected in the Offering Memorandum and the Management Presentations. For purposes of this Section 8.9, the term "affiliation" shall mean any direct or indirect interest in such Person or enterprise, whether as an investor, partner, stockholder, operator, lender, trustee, joint venture contributor, licensor or consultant (other than passive investments by Isis of less than [***]% of the outstanding equity securities of any entity listed for trading on a national stock exchange or investments in less than [***]% of the outstanding equity securities by Isis in a Person engaged in drug discovery, development or commercialization).

(b) Pre-Existing Business. Notwithstanding the foregoing, if a Person becomes an Affiliate of Isis after the Closing Date, and such Person was engaged in a line of business that on or before the time such Person became an Affiliate of Isis, competed with the Business as conducted on and prior to the Closing Date and as contemplated by Ibis and Isis to be

conducted after the Closing Date, as reflected in the Offering Memorandum and Management Presentations (a "Pre-Existing Business"), then the provisions of Section 8.9(a) will not apply to such Pre-Existing Business if (i) such third party does not [***] and (ii) appropriate protective measures and procedures are established by Isis and its Affiliates and such Person and its Affiliates to protect and safeguard the confidentiality of Abbott and Ibis Confidential Information.

(c) No Solicitation of AMI Employees. During the period from the date hereof to and including the [***] anniversary of the Closing Date (the "Nonsolicitation Period"), Isis (and until the Closing, Ibis) shall not and shall not permit any of their respective Representatives to directly or indirectly, (i) without the prior written consent of AMI, induce or attempt to induce any employee of AMI or any member of the Abbott Transaction Team to leave the employ of AMI or the applicable Abbott Affiliate, or in any way interfere with the relationship between AMI or the applicable Abbott Affiliates and any employee of AMI or any member of the Abbott Transaction Team, or Known consultant or independent contractor thereof or (ii) without the prior written consent of AMI, hire directly or through another entity any employee of AMI or any member of the Abbott Transaction Team or any Person who was an employee of AMI or a member of the Abbott Transaction Team who was employed by Abbott or any of its Affiliates during the [***] months prior to the date of such hiring, in each case to work for Isis or Ibis.

(d) No Solicitation of Ibis or Isis Employees. During the Nonsolicitation Period with respect to employees of Isis and until the Closing with respect to employees of Ibis, AMI and its Affiliates will cause AMI and the members of the Abbott Transaction Team not to, directly or

indirectly, (i) without the prior written consent of Isis or Ibis (as the case may be), induce or attempt to induce any employee of Isis or Ibis to leave the employ of Isis or Ibis, or in any way interfere with the relationship between Isis or Ibis and any of their respective employees, or Known consultant or independent contractor thereof or (ii) without the prior written consent of Isis or Ibis (as the case may be), hire directly or through another entity any employee of Isis or Ibis or any Person who was an employee of Isis or Ibis who was employed by Isis or Ibis during the [***] months prior to the date of such hiring, in each case to work for AMI.

(e) No Solicitation of Ibis Employees. During the Nonsolicitation Period, Isis shall not and shall not permit any of its Representatives to directly or indirectly (i) without the prior written consent of AMI, induce or attempt to induce any employee of Ibis to leave the employ of Ibis, or in any way interfere with the relationship between Ibis and any employee, consultant or independent contractor thereof, (ii) without the prior written consent of AMI, hire directly or through another entity any employee of Ibis or any Person who was an employee of Ibis during the [***] months prior to the date of such hiring or (iii) induce or attempt to induce any customer, supplier, licensee, licensor or other business relation of Ibis, AMI or any of their respective Affiliates or the Business, to cease doing business with Ibis, AMI or any of their respective Affiliates or the Business.

For purposes of Sections 8.9(c), 8.9(d) and 8.9(e), "recruit," "solicit" or "induce" shall not be deemed to mean (i) circumstances where an employee, consultant or independent contractor or former employee, consultant or independent contractor initiates contact with a Party with regard

to possible employment, or (ii) general solicitations of employment not specifically targeted at specific employees of a Party, including responses to general advertisements.

Notwithstanding anything in this Section 8.9 to the contrary, if at any time a court holds that the restrictions stated in Section 8.9(a), Section 8.9(c), Section 8.9(d) or Section 8.9(e) or any part of any of the foregoing are unreasonable or otherwise unenforceable under circumstances then existing, the Parties hereto agree that the maximum period, scope or geographical area determined to be reasonable under such circumstances by such court will be substituted for the stated period, scope or area. The Parties acknowledge and agree that money damages may not be an adequate remedy for any breach or threatened breach of the provisions of Section 8.9(a), Section 8.9(c), Section 8.9(d) or Section 8.9(e) and that, in such event, any Party or its successors or assigns may, in addition to any other rights and remedies existing in its or their favor, apply to any court of competent jurisdiction for specific performance, injunctive and/or other relief in order to enforce or prevent any violations of the provisions of this Section 8.9 (including, if the court so determines, the extension of the Noncompete Period or the Nonsolicitation Period, as applicable, by a period equal to the length of court proceedings necessary to stop such violation). Any injunction shall be available without the posting of any bond or other security. In the event of an alleged breach or violation by any Party or any of their respective Representatives of any of the provisions of this Section 8.9, the Noncompete Period or the Nonsolicitation Period, as applicable will be tolled until such alleged breach or violation is resolved. The Parties agree that the restrictions contained in this Section 8.9 are reasonable in all respects.

8.10 Access to Books and Records. After the Closing, Isis will permit AMI and its representatives, and AMI will permit Isis and its representatives, to have reasonable access upon prior notice and at reasonable times, and in a manner so as not to interfere with the normal business operations of the other Party, to all books, records (including Tax records), contracts and documents of or pertaining to Ibis.

8.11 Employee and Related Matters.

(a) Ibis Employees. All employees of Ibis employed as of the Closing Date (the "Ibis Employees") shall, as of the Closing, receive compensation and benefits from Abbott that are substantially comparable, in the aggregate, to the compensation and benefits received by other similarly-situated employees of Abbott based on Abbott's evaluation of the nature and scope of such employee's duties, principal location where those duties are performed, grade level and performance. To facilitate Abbott's obligations to provide such compensation and benefits under this Section 8.11, Isis shall provide AMI promptly, upon AMI's request, but in any event, no less than [***] prior to the Closing Date (and again on the Closing Date) a true, complete and accurate list of each Ibis Employee, including the date of employment and title or job position of each Ibis Employee, information regarding pay and benefits, including, but not limited to, the total annual salary, wages, bonus or other compensation of each Ibis Employee, and, with respect to any Ibis Employees who are inactive Ibis Employees (as defined in Section 8.11(f)), the date such inactive employee changed from active to inactive status, the reason for such inactive status and, if applicable, the anticipated date of return to active employment. Ibis Employees shall be employees at will, subject to Abbott's employment policies and nothing herein shall be construed to limit Abbott's ability to (a) terminate or alter the employment terms of any Ibis Employee for any reason, including without cause, or (b) modify, amend or terminate

any employee benefit plan, policy or arrangement, except that neither Abbott nor AMI nor Ibis may make any material amendment to the terms and provisions of the Permitted Employee Compensation Plan.

(b) WARN. Isis covenants and agrees to cause Ibis to comply, if applicable, with all requirements specified under the Worker Adjustment and Retraining Notification Act of 1988 (the "WARN Act") or any similar or successor federal, state or local law, including the provision of appropriate notice to affected employees with respect to any "employment loss" (as defined in the WARN Act) that occurs on or prior to the Closing Date. Except as set forth on Schedule 8.11(b), no Ibis Employee has suffered an "employment loss" during the ninety (90)-day period prior to the date hereof. Isis shall update Schedule 8.11(b) as necessary to reflect all "employment losses" between the date hereof and prior to the Closing Date.

(c) COBRA. Isis shall retain responsibility for all liability for any health care continuation coverage or notice requirement under Section 4980B of the Code and Part G of Subtitle B of Title 1 of ERISA with respect to any Plan, including with respect to all former employees of Ibis or the Business, who are former employees thereof as of the Closing.

(d) Retirement Plans. Prior to or on the Closing Date, Isis and/or Ibis shall make all matching contributions and a pro-rated portion of any profit sharing contributions that would otherwise be made for the plan year (without regard to any year-end employment requirements) with respect to the Ibis Employees' contributions to any Plan that is intended to be qualified under Section 401(a) of the Code (the "Isis Retirement Plans"). Isis shall prior to the Closing: (A) amend each Isis Retirement Plan to cause the account balances or accrued benefits of Ibis Employees to be fully vested as of the Closing Date and (B) amend each Isis Retirement Plan that includes a cash or deferred arrangement under Section 401(k) of the Code to permit Ibis

Employees with an outstanding plan loan to roll over such loan to Abbott's 401(k) plan. Abbott will cause its 401(k) plan to accept a direct rollover of the Ibis Employees' 401(k) account balance, including a direct rollover of any outstanding plan loan.

(e) Payroll Tax Reporting. Ibis, Isis and AMI agree that payroll reporting of the Ibis Employees will be treated in accordance with the Alternate Procedure set forth in Section 5 of Revenue Procedure 2004-53.

(f) Retention of Liability. Isis shall be solely responsible for, and retain all liabilities with respect to and Isis shall retain, bear and discharge all liabilities and obligations with respect to all inactive Ibis Employees until such time as the inactive Ibis Employee returns to active employment with Ibis. Isis shall be solely responsible for, and retain all liabilities with respect to, all wages, salaries, commissions, bonuses, vacation pay and other compensation payable to any Ibis Employee for all periods through and including the Closing Date. AMI shall not assume liability for any retention, severance, change-of-control or similar agreements between Isis and any of the Ibis Employees, and Isis shall retain or assume liability for all obligations under any such retention, severance, change-of-control or similar agreements. For purposes of this Section 8.11, an "inactive Ibis Employee" shall mean any employee of Ibis who, as of the Closing Date, is on any type of leave of absence or who has been otherwise

continuously absent from work with Ibis for any reason for longer than five (5) working days, other than for approved paid vacation.

(g) Full-Time Equivalents. From and after the date hereof, Isis and Ibis shall cause the number of full-time equivalent employees (not including temporary employees and consultants) of Ibis to be not greater than 70 in the aggregate and to be not less than 56 in the aggregate.

(h) No Third Party Rights. Nothing in this Agreement, express or implied, shall create a contract of employment with any Ibis Employee or a third party beneficiary relationship or otherwise amend or create any employee benefit plan of AMI or Ibis or confer any benefit, entitlement, or right upon any person or entity other than the parties hereto or result in AMI or Ibis having any liability under any Plan (other than Ibis' liability with respect to the Permitted Employee Compensation Plan).

8.12 Consolidated Return. From and after the date hereof, Isis will file a consolidated Tax Return with respect to itself and Ibis in lieu of separate Tax Returns with respect to income Tax imposed by Chapter 1 of the Code for the Tax year beginning January 1, 2007 through and including the Closing unless the provisions of the Code shall have been amended after the date hereof to disallow the filing of such consolidated Tax Returns. In the event of an Internal Revenue Service audit of Isis arising out or related to the consolidation of Ibis and Isis in such consolidated Tax Return, Isis will promptly (but in any event within [***]) notify AMI of such audit and allow AMI to participate and advise Ibis and Isis in connection with such audit.

8.13 Isis Intellectual Property License.

(a) To the extent Isis has not as of the Closing Date granted rights preventing Isis from making any further license grants, Isis hereby grants Ibis a worldwide, fully-paid, royalty free, non-exclusive license (without the right to grant sublicenses, except to purchasers, distributors or resellers of Products to use, sell or resell, the amounts of Products purchased) under the Isis Licensed Intellectual Property to make, have made, import, use (in any field of use, including research performed internally and with collaborators, and in the sale of services), offer for sale, and sell Products. This license is transferable by Ibis to its Affiliates or to a successor in interest to Ibis without the prior written consent of Isis.

(b) Additionally, upon Ibis' request, Isis shall grant Ibis worldwide, fully-paid, royalty free, non-exclusive licenses (without the right to grant sublicenses, except to purchasers, distributors or resellers of Products to use, sell or resell, the amounts of Products purchased) to any [***] make, have made, import, use (in any field of use, including research performed internally and with collaborators, and in the sale of services), offer for sale and sell Products, to the extent Isis has not previously granted rights preventing Isis from granting such licenses to Ibis. This right to license Isis' Intellectual Property is transferable by Ibis to its Affiliates or to a successor in interest to Ibis without the prior written consent of Isis.

(c) Until [***], Isis and its Affiliates shall not license any [***] for use with a [***].

Section 9. TERMINATION.

9.1 Termination. AMI or Isis may terminate this Agreement as follows:

(a) by mutual written consent at any time prior to the Closing;

(b) by giving written notice to the other at any time prior to Closing if there has been a material misrepresentation or breach on the part of the other Party of the representations, warranties or covenants set forth in this Agreement, which breach cannot be or has not been cured, in all material respects, within [***] after the giving of written notice of such breach to AMI or Isis, as applicable;

(c) if events have occurred which have made it impossible to satisfy a condition precedent to the terminating Party's obligations to consummate the transactions contemplated hereby unless such terminating Party's willful breach of this Agreement has caused the condition to be unsatisfied;

(d) by giving written notice to the other Party at any time prior to the Closing if the Closing shall not have occurred on or before the date that is [***] from the date hereof or, in the event that the applicable waiting periods (and any extensions thereof) under the HSR Act have not expired or otherwise been terminated (whether as a result of a "second request" or otherwise), the date that is [***] from the date hereof; provided that neither AMI nor Isis shall be entitled to terminate this Agreement pursuant to this Section 9.1(d) if such Party's willful breach of this Agreement has prevented the consummation of the transactions contemplated hereby at or before such time.

9.2 Effect of Termination. In the event of termination of this Agreement by either AMI or Isis as provided in Section 9.1, this Agreement shall forthwith become null and void and there shall be no liability on the part of any Party to any other Party under this Agreement, except that

the provisions of Section 1, this Section 9.2, Section 8.3, Section 8.4, Section 8.8, and Section 10 shall continue in full force and effect, except that nothing herein shall relieve any Party from liability for any breach of this Agreement prior to such termination.

Section 10. MISCELLANEOUS.

10.1 No Third Party Beneficiaries. This Agreement shall not confer any rights or remedies upon any Person other than the Parties and their respective successors and permitted assigns.

10.2 Entire Agreement. This Agreement, the Exhibits and Schedules hereto, the Transaction Documents and the other documents delivered pursuant hereto or referred to herein constitute the full and entire understanding and agreement between the Parties with regard to the subject hereof and no party will be liable for or bound to any other in any manner by any oral or written representations, warranties, covenants and agreements except as specifically set forth herein or therein. From and after the Closing, the Investment Documents shall terminate and be of no further force or effect except that such termination shall not relieve any Party from liability for any breach of such agreements prior to such termination.

10.3 Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the Parties and their respective successors and permitted assigns. No Party may assign either this Agreement or any of its rights, interests or obligations hereunder without the prior written approval of the other Party; *provided* that AMI may (x) assign any or all of its rights and interests hereunder to one or more of its Affiliates, (y) designate one or more of its Affiliates to perform its obligations hereunder (in any or all of which cases AMI nonetheless shall remain responsible for the performance of all of its obligations hereunder), and (z) assign any or all of its rights and interests hereunder in connection with a Change of Control of AMI. Except as otherwise expressly provided herein, the provisions hereof shall inure to the benefit of, and be binding upon and be enforceable by the Parties and their respective successors, assigns, heirs, executors and administrators.

10.4 Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original but all of which together will constitute one and the same instrument. This Agreement and any signed agreement or instrument entered into in connection with this Agreement, and any amendments hereto or thereto, to the extent signed and delivered by means of a facsimile machine or other electronic means, shall be treated in all manner and respects as an original agreement or instrument and shall be considered to have the same binding legal effect as if it were the original signed version thereof delivered in person. At the request of any party hereto or to any such agreement or instrument, each other party hereto or thereto shall re-execute original forms thereof and deliver them to all other parties. No party hereto or to any such agreement or instrument shall raise the use of a facsimile machine or other electronic means to deliver a signature or the fact that any signature or agreement or instrument was transmitted or communicated through the use of a facsimile machine or other electronic means as a defense to the formation of a contract and each such party forever waives any such defense.

10.5 Headings. The section headings contained in this Agreement are inserted for convenience only and shall not affect in any way the meaning or interpretation of this Agreement.

10.6 Notices. All notices, requests, demands, claims, and other communications hereunder will be in writing. Any notice, request, demand, claim, or other communication hereunder shall be deemed duly given (i) when delivered on a Business Day, if personally delivered or sent by facsimile or other electronic means (subject to confirmation of such delivery), on such Business Day, (ii) when delivered other than on a Business Day, if personally delivered or sent by facsimile or other electronic means (subject to confirmation of such delivery), on the first Business Day after dispatch, (iii) on the Business Day after dispatch, if sent by nationally-recognized overnight courier, and (iv) on the third Business Day following the date of mailing, if sent by mail, in each case, addressed to the intended recipient as set forth below:

If to Ibis, to:

Ibis Biosciences Inc.
1896 Rutherford Road
Carlsbad, CA 92008
Attention: President
Facsimile: (760) 603-4653

If to Isis, to:

Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008
Attention: Chief Financial Officer
Facsimile: (760) 603-4650

with a copy to:

1896 Rutherford Road
Carlsbad, CA 92008
Attention: General Counsel
Facsimile: (760) 268-4922

If to AMI:

Abbott Molecular Inc.

c/o Abbott Laboratories
Corporate Transactions and Medical Products Legal Operations
Dept. 322, Bldg. AP6A
100 Abbott Park Road
Abbott Park, IL 60064-6010
Attention: Vice President and Associate General Counsel
Facsimile: (847) 938-1206

with a copy to:

Kirkland & Ellis LLP
200 East Randolph Drive
Chicago, IL 60601
Attn: R. Scott Falk, P.C.
R. Henry Kleeman
Facsimile: (312) 861-2200

Any Party may send any notice, request, demand, claim or other communication hereunder to the intended recipient at the address set forth above using any other means, but no such notice, request, demand, claim or other communication shall be deemed to have been duly given unless and until it actually is received by the intended recipient. Any Party may change the address to which notices, requests, demands, claims and other communications hereunder are to be delivered by giving the other Party notice in the manner herein set forth.

10.7 Governing Law. This Agreement shall be governed by and construed in accordance with the domestic laws of the State of Delaware without giving effect to any choice

or conflict of law provision or rule (whether of the State of Delaware or any other jurisdiction) that would cause the application of the laws of any jurisdiction other than the State of Delaware.

10.8 Alternative Dispute Resolution Procedure. The Parties recognize that from time to time a dispute may arise relating to a Party's rights or obligations under this Agreement or the other Transaction Documents. The Parties agree that any such dispute shall be resolved by the Alternative Dispute Resolution ("ADR") provisions set forth in Exhibit C the result of which shall be binding upon the Parties.

10.9 Amendments and Waivers. No amendment of any provision of this Agreement shall be valid unless the same shall be in writing and signed by AMI and Isis. No waiver by any Party of any default, misrepresentation, or breach of warranty or covenant hereunder, whether intentional or not, shall be deemed to extend to any prior or subsequent default, misrepresentation or breach of warranty or covenant hereunder or affect in any way any rights arising by virtue of any prior or subsequent such occurrence.

10.10 Delays or Omissions. It is agreed that no delay or omission to exercise any right, power or remedy accruing to any Party, upon any breach, default or noncompliance by another party under a Transaction Document or otherwise, will impair any such right, power or remedy, nor will it be construed to be a waiver of any such breach, default or noncompliance, or any acquiescence therein, or of or in any similar breach, default or noncompliance thereafter occurring. It is further agreed that any waiver, permit, consent or approval of any kind or character on any Party's part of any breach, default or noncompliance under a Transaction Document or otherwise or any waiver on such Party's part of any provisions or conditions of a Transaction Document, or otherwise must be in writing and will be effective only to the extent specifically set forth in such writing. All remedies, either under a Transaction Document, Ibis' Certificate of Incorporation, bylaw, or otherwise afforded to any party, will be cumulative and not alternative.

10.11 Incorporation of Exhibits and Schedules. The exhibits and Schedules identified in this Agreement are incorporated herein by reference and made a part hereof. The Parties acknowledge and agree that (i) the Disclosure Schedules are arranged in sections corresponding to the sections and paragraphs of this Agreement and the disclosures therein qualify the specifically referenced corresponding representations and warranties of the Parties contained in this Agreement, (ii) to the extent this Agreement requires disclosure of any matter, such matter disclosed pursuant to one provision, subprovision, section or subsection of the Disclosure Schedules shall be deemed disclosed only to the extent actually disclosed with respect to the specific provision, subprovision, section or subsection of the Disclosure Schedule that it is actually disclosed pursuant to and (iii) section numbers and titles inserted in the Disclosure Schedules are for convenience of reference only and shall to no extent have the effect of amending or changing the express description of such sections of the Disclosure Schedules as set forth in this Agreement. Information set forth in each section of the Disclosure Schedules specifically refers to the section of this Agreement to which such information is responsive, and such information shall not be deemed to have been disclosed with respect to any statement made in any other section of this Agreement. Any capitalized terms used in any Schedule but not otherwise defined therein shall have the meanings ascribed to such terms in this Agreement.

10.12 Construction. The Parties acknowledge and agree that they have been represented by counsel during the negotiation, preparation and execution of this Agreement and, therefore, waive the application of any Law or rule of construction providing that ambiguities in an agreement or other document shall be construed against the Party drafting such agreement or document. Where specific language is used to clarify by example a general statement contained herein, such specific language shall not be deemed to modify, limit or restrict in any manner the construction of the general statement to which it relates. When the context so requires the word "or" when used herein shall mean "and/or." All pronouns contained herein, and any variations thereof, will be deemed to refer to the masculine, feminine or neutral, singular or plural, as the identity of the Parties hereto may require. Other than with respect to Section 3.2, Section 4.1 and the preamble to Section 5.1, the words, "provided to," "delivered" or "made available" or words of similar import when used in this Agreement to refer to obligations of Isis and/or Ibis to "provide," "deliver" or "make available" materials to AMI mean "made available in the online dataroom maintained by Isis at '[***]' at least three (3) Business Days prior to the date hereof". Unless otherwise provided therein, when used in any Transaction Document or Schedule, "Dollars" or "$" means the lawful currency of the United States of America.

10.13 Remedies. Each of the Parties acknowledges and agrees that the other Party would be damaged irreparably in the event any of the provisions of this Agreement are not performed in accordance with their specific terms or otherwise are breached. Accordingly, each of the Parties agrees that, subject to Section 10.8 the other Party shall be entitled to an injunction or injunctions to prevent breaches of the provisions of this Agreement and to enforce specifically this Agreement and the terms and provisions hereof in any action instituted in any court of the United States or any state thereof having jurisdiction over the Parties and the matter (subject to Section 10.8 above), in addition to any other remedy to which they may be entitled, at law or in equity.

10.14 Severability. In the event that any provision of this Agreement, or the application thereof, becomes or is declared by a court of competent jurisdiction to be illegal, void or unenforceable, the remainder of this Agreement shall continue in full force and effect and the application of such provision to other Persons or circumstances shall be interpreted so as reasonably to effect the intent of the Parties hereto. The Parties further agree to replace such void or unenforceable provision of this Agreement with a valid and enforceable provision that will achieve, to the extent possible, the economic, business and other purposes of such void or unenforceable provision.

10.15 No Other Compensation.

The Parties hereby agree that the terms of the Transaction Documents fully define all consideration, compensation and benefits, monetary or otherwise, to be paid, granted or delivered by Isis or Ibis to AMI or Abbott and by AMI or Abbott to Isis or Ibis in connection with the transactions contemplated herein and therein. Except pursuant to the Permitted Employee Compensation Plan, no Party previously has paid or entered into any other commitment to pay, whether orally or in writing, any employee of any other Party, directly or indirectly, any consideration, compensation or benefits, monetary or otherwise, in connection with the transactions contemplated in the Transaction Documents.

* * * * *

IN WITNESS WHEREOF, the Parties hereto have executed this Stock Purchase Agreement as of the date first above written.

ISIS PHARMACEUTICALS, INC.

By: _____
Name: _____
Title: _____

IBIS BIOSCIENCES, INC.

By: _____
Name: _____
Title: _____

ABBOTT MOLECULAR INC.

By: _____
Name: _____
Title: _____

SIGNATURE PAGE TO STOCK PURCHASE AGREEMENT

LIST OF EXHIBITS

EXHIBIT A

TRANSITION SERVICES AGREEMENT

EXHIBIT B

ESCROW AGREEMENT

EXHIBIT C

ADR PROCEDURE

To begin the ADR process, a Party first must send written notice of the dispute to the other Party for attempted resolution by good faith negotiations between their respective presidents (or their designees) of the affected subsidiaries, divisions, or business units within twenty-eight (28) days after such notice is received (all references to "days" in this ADR provision are to calendar days). If the matter has not been resolved within twenty-eight (28) days after the notice of dispute, or if the parties fail to meet within such twenty-eight (28) days, either Party may initiate an ADR proceeding as provided herein. The parties shall have the right to be represented by counsel in such a proceeding.

1. To begin an ADR proceeding, a Party shall provide written notice to the other Party of the issues to be resolved by ADR. Within fourteen (14) days after its receipt of such notice, the other Party may, by written notice to the Party initiating the ADR, add additional issues to be resolved within the same ADR.

2. Within twenty-one (21) days following the initiation of the ADR proceeding, the Parties shall select a mutually acceptable independent, impartial and conflicts-free neutral to preside in the resolution of any disputes in this ADR proceeding. If the Parties are unable to agree on a mutually acceptable neutral within such period, each Party will select one independent, impartial and conflicts-free neutral and those two neutrals will select a third independent, impartial and conflicts-free neutral within ten (10) days thereafter. None of the neutrals selected may be current or former employees, officers or directors of either Party, its Subsidiaries or Affiliates or a current consultant or independent contractor of either Party or its Affiliates.

3. No earlier than twenty-eight (28) days or later than fifty-six (56) days after selection, the neutral(s) shall hold a hearing to resolve each of the issues identified by the Parties. The ADR proceeding shall take place at a location agreed upon by the Parties. If the Parties cannot agree, the neutral(s) shall designate a location other than the principal place of business of either Party or any of their Subsidiaries or Affiliates.

4. At least seven (7) days prior to the hearing, each Party shall submit the following to the other Party and the neutral(s):

(a) a copy of all exhibits on which such Party intends to rely in any oral or written presentation to the neutral;

(b) a list of any witnesses such Party intends to call at the hearing, and a short summary of the anticipated testimony of each witness;

(c) a proposed ruling on each issue to be resolved, together with a request for a specific damage award or other remedy for each issue. The proposed rulings and remedies shall not contain any recitation of the facts or any legal arguments and shall not exceed one (1) page per issue. The Parties agree that neither side shall seek as part of its remedy any punitive damages.

(d) a brief in support of such Party's proposed rulings and remedies, provided that the brief shall not exceed twenty (20) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

Except as expressly set forth in subparagraphs 4(a) - 4(d), no discovery shall be required or permitted by any means, including depositions, interrogatories, requests for admissions, or production of documents.

5. The hearing shall be conducted on two (2) consecutive days and shall be governed by the following rules:

(a) Each Party shall be entitled to five (5) hours of hearing time to present its case. The neutral shall determine whether each Party has had the five (5) hours to which it is entitled.

(b) Each Party shall be entitled, but not required, to make an opening statement, to present regular and rebuttal testimony, documents or other evidence, to cross-examine witnesses, and to make a closing argument. Cross-examination of witnesses shall occur immediately after their direct testimony, and cross-examination time shall be charged against the Party conducting the cross-examination.

(c) The Party initiating the ADR shall begin the hearing and, if it chooses to make an opening statement, shall address not only issues it raised but also any issues raised by the responding Party. The responding Party, if it chooses to make an opening statement, also shall address all issues raised in the ADR. Thereafter, the presentation of regular and rebuttal testimony and documents, other evidence, and closing arguments shall proceed in the same sequence.

(d) Except when testifying, witnesses shall be excluded from the hearing until closing arguments.

(e) Settlement negotiations, including any statements made therein, shall not be admissible under any circumstances. Affidavits prepared for purposes of the ADR hearing also shall not be admissible. As to all other matters, the neutral(s) shall have sole discretion regarding the admissibility of any evidence.

6. Within seven (7) days following completion of the hearing, each Party may submit to the other Party and the neutral(s) a post-hearing brief in support of its proposed rulings and remedies, provided that such brief shall not contain or discuss any new evidence and shall not exceed ten (10) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

7. The neutral(s) shall rule on each disputed issue within fourteen (14) days following completion of the hearing. Such ruling shall adopt in its entirety the proposed ruling and remedy of one of the Parties on each disputed issue but may adopt one Party's proposed rulings and remedies on some issues and the other Party's proposed rulings and remedies on other issues. The neutral(s) shall not issue any written opinion or otherwise explain the basis of the ruling.

8. The neutral(s) shall be paid a reasonable fee plus expenses. These fees and expenses, along with the reasonable legal fees and expenses of the prevailing Party (including all expert witness fees and expenses), the fees and expenses of a court reporter, and any expenses for a hearing room, shall be paid as follows:

(a) If the neutral(s) rule(s) in favor of one Party on all disputed issues in the ADR, the losing Party shall pay 100% of such fees and expenses.

(b) If the neutral(s) rule(s) in favor of one Party on some issues and the other Party on other issues, the neutral(s) shall issue with the rulings a written determination as to how such fees and expenses shall be allocated among the Parties. The neutral(s) shall allocate fees and expenses in a way that bears a reasonable relationship to the outcome of the ADR, with the Party prevailing on more issues, or on issues of greater value or gravity, recovering a relatively larger share of its legal fees and expenses.

9. The rulings of the neutral(s) and the allocation of fees and expenses shall be binding, non-reviewable, and non-appealable, and may be entered as a final judgment in any court having jurisdiction.

10. Except as provided in paragraph 9 or as required by law, the existence of the dispute, any settlement negotiations, the ADR hearing, any submissions (including exhibits, testimony, proposed rulings, and briefs), and the rulings shall be deemed Confidential Information. The neutral(s) shall have the authority to impose sanctions for unauthorized disclosure of Confidential Information.

EXHIBIT D

PERMITTED EMPLOYEE COMPENSATION PLAN

AMI and Isis will mutually agree on the [***]. The money available for such package, in the aggregate, will be $[***], a portion of which (approximately $[***] assuming normal employee turnover rates) would be [***]. Any funds [***] would be released to [***].

EXHIBIT E

PRESS RELEASE

EXHIBIT B

STOCK SUBSCRIPTION AGREEMENT

AMONG

IBIS BIOSCIENCES, INC.

ISIS PHARMACEUTICALS, INC.

AND

ABBOTT MOLECULAR INC.

[ ], 2008

STOCK SUBSCRIPTION AGREEMENT

THIS STOCK SUBSCRIPTION AGREEMENT (this "Agreement") is made and entered into as of this [ ] day of [ ], 2008, by and among Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"), Ibis Biosciences, Inc., a Delaware corporation and majority owned subsidiary of Isis ("Ibis"), and Abbott Molecular, Inc., a Delaware corporation ("AMI"). Isis, Ibis and AMI are sometimes referred to herein individually as a "Party," and collectively as the "Parties."

RECITALS

WHEREAS, on January 30, 2008, the Parties entered into a Strategic Alliance Master Agreement (the "Master Agreement") and certain other Investment Documents, pursuant to which, among other things, AMI acquired the Shares from Ibis;

WHEREAS, in connection with the transactions contemplated by the Investment Documents, Ibis granted a Subscription Right to AMI and AMI acquired the Subscription Right from Ibis on the terms set forth in the Call Option Agreement; and

WHEREAS, on [ ], 2008, in accordance with the terms and provisions of the Call Option Agreement, AMI has exercised the Subscription Right and desires to acquire the Additional Shares pursuant to the terms hereof.

AGREEMENT

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, and covenants set forth herein and in the Master Agreement and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

SECTION 1. Definitions.

Capitalized terms used and not otherwise defined herein have the meanings ascribed to such terms in the Master Agreement.

SECTION 2. Subsequent Closing; Delivery And Payment.

2.1 Subsequent Closing. The closing of the sale and purchase of the Additional Shares under this Agreement (the "Subsequent Closing") will take place at 1:00 p.m. on the date hereof, at the offices of Kirkland & Ellis LLP, 200 E. Randolph Dr. Chicago, IL 60601 or at such other time or place as the Parties may mutually agree (such date is hereinafter referred to as the "Subsequent Closing Date").

2.2 Delivery. Subject to and upon the terms and conditions set forth in this Agreement, and in reliance upon the respective representations and warranties made herein by each of the Parties, at the Subsequent Closing:

(a) Ibis shall issue, sell, convey, assign, transfer and deliver to AMI a certificate representing the Additional Shares sufficient to vest in AMI legal and beneficial ownership of the Additional Shares, free and clear of all Encumbrances; and

(b) AMI shall purchase, acquire and accept the Additional Shares from Ibis for $20,000,000, paid to Ibis via wire transfer of immediately available funds to an account designated by Ibis in writing.

SECTION 3. Representations And Warranties of the Parties.

3.1 Representations and Warranties of Ibis and Isis. As a material inducement to AMI to enter into this Agreement, except as set forth in the corresponding Section of the Disclosure Schedules delivered to AMI herewith on the date hereof (the "Disclosure Schedules"), Ibis and Isis each hereby jointly and severally represent and warrant as follows:

(a) Power and Authority. Each of Ibis and Isis (i) has the power, authority and the legal right to enter into this Agreement and to perform its obligations hereunder and (ii) has taken all necessary action required to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder.

(b) Enforceability. This Agreement has been duly executed and delivered on behalf of Ibis and Isis and constitutes a legal, valid and binding obligation of each such Party and is enforceable against each such Party in accordance with its terms subject to the effects of bankruptcy, insolvency or other Laws of general application affecting the enforcement of creditor rights.

(c) Governmental Authority; Consents. All necessary consents, approvals and authorizations of all Governmental Authorities and other parties required to be obtained by Ibis and Isis in connection with the execution and delivery of this Agreement and the performance of their obligations hereunder have been obtained.

(d) No Conflicts. The execution and delivery of this Agreement by each of Ibis and Isis and the performance of each such Party's obligations hereunder, with or without the passage of time or giving of notice, (i) do not and will not conflict with or violate any requirement of Applicable Law or any provision of the certificate of incorporation, bylaws or any similar instrument of such Party, as applicable, (ii) do not and will not require any notice, conflict with, violate, or breach or constitute a default or require any consent or give rise to any termination or acceleration right or the creation of any Encumbrance on the Additional Shares or any of the properties or assets of Ibis under, any contractual obligation by which such Party is bound or subject to and (iii) do not and will not cause the suspension, revocation, impairment, forfeiture or nonrenewal of any License applicable to Ibis, the Business or any of Ibis' operations, assets or properties.

(e) Due Organization; Qualification. Each of Ibis and Isis is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, with full corporate power and authority to enter into this Agreement. Except as would not reasonably be expected to have a Material Adverse Effect, Ibis has obtained and currently maintains all qualifications to do business as a foreign corporation in all jurisdictions in which

the character of the Business requires it to be so qualified. Ibis has all requisite power and authority and all authorizations and Licenses necessary to own, operate or conduct the Business.

(f) Capitalization; Voting Rights.

(i) The authorized Capital Stock of Ibis consists of 1,228,501 shares of Common Stock, par value $0.001 per share, 1,114,251 shares of which are issued and outstanding and 1,000,000 of which are held by Isis (the "Remaining Shares") and 114,251 of which are held by AMI.

(ii) The issued and outstanding Capital Stock of Ibis as of the Subsequent Closing will consist exclusively of the Shares, the Additional Shares and the Remaining Shares. Except as set forth in the Investor Rights Agreement, Ibis does not have any obligations to issue or redeem any shares of Capital Stock, other than with respect to the Additional Shares and Ibis has not issued any Capital Stock other than the Shares and the Remaining Shares. No Capital Stock issued by Ibis is listed on any stock exchange or unregulated market. Other than the Investment Documents, there are no agreements with Isis or Ibis or any other Person with respect to the voting or Transfer of the Capital Stock.

(iii) The Additional Shares are: (A) duly authorized, validly issued, fully paid and nonassessable; (B) issued in compliance with all applicable state and federal Laws concerning the issuance of Capital Stock; and (C) free and clear of all Encumbrances other than the rights and obligations set forth in the Investor Rights Agreement; *provided*, that the Additional Shares may be subject to restrictions on Transfer set forth in the Investor Rights Agreement and under state and/or federal securities Laws as set forth herein or as otherwise required by such Laws at the time a Transfer is proposed.

(iv) Neither the sale of the Additional Shares to AMI hereunder nor the sale of the Remaining Shares to AMI under the Acquisition Agreement is subject to any preemptive rights, rights of first refusal or similar rights.

(g) Compliance with Other Instruments. Neither Ibis nor, with respect to the Business, Isis is in violation or default of any term of its charter documents, each as amended, or of any provision of any Contract to which it is party or by which the Business is bound or of any judgment, decree, order or writ.

(h) Financial Statements. Schedule 3.1(t) attached hereto contains the following financial statements (collectively the "Financial Statements"): [(i) the profit and loss statement for Ibis for the fiscal year ended December 31, 2007, (ii) the profit and loss statement for Ibis and the related balance sheet (the "Most Recent Balance Sheet") for the [three] month period ended [March 31, 2008].(1) The Financial Statements have been prepared in accordance with GAAP throughout the periods covered thereby, present fairly in all material respects the financial condition of Ibis or the Division (as the case may be) as of such dates and the results of operations of Ibis or the Division (as the case may be) for such periods, and are materially

(1) The most recent financial statements available upon exercise of the Subscription Rights will be referenced in this Section.

correct and complete and consistent with the books and records of Ibis (which books and records are materially correct and complete).

(i) Customers and Suppliers. Schedule 3.1(z) accurately sets forth a list of the Business' top ten customers by revenue for the fiscal year ended December 31, 2007 and the [three] month period ended [March 31, 2008]. Except as set forth on Schedule 3.1(z), neither Isis nor Ibis has received any indication from any material customer of the Business or any Governmental Authority to the effect that, and neither Isis nor Ibis has any reason to believe that, such customer or Governmental Authority will in the future stop, or materially decrease the rate of buying products or services from the Business. Schedule 3.1(z) also accurately sets forth a list of the Business' top ten suppliers by dollar amount for the fiscal year ended December 31, 2007 and the [three] month period ended [March 31, 2008].(2) Except as set forth on Schedule 3.1(z), neither Isis nor Ibis has received any indication from any material supplier of the Business to the effect that, and neither Isis nor Ibis has any reason to believe that, such supplier will stop or materially decrease the rate of providing products or services to the Business and its customers. Neither Isis nor Ibis is involved in any material dispute with any customer or supplier of or to the Business.

(j) No Material Adverse Effect. Since the Financing Closing, there has been no Material Adverse Effect.

(k) Master Agreement. The representations and warranties made by Isis and Ibis in the Master Agreement are true and correct as of the date hereof, except that the representations and warranties in Sections 3.1(t) and 3.1(z) of the Master Agreement are true and correct as restated as set forth in Sections 3.1(h) and 3.1(i), respectively, above. Ibis and Isis have complied with and performed the covenants and agreements set forth in the Investment Documents in all material respects as of the date hereof.

(l) Offering Valid. Assuming the accuracy of the representations and warranties of AMI contained in Section 3.2 hereof, the offer, sale and issuance of the Additional Shares is exempt from the registration requirements of the Securities Act, and have been registered or qualified (or are exempt from registration and qualification) under the registration, permit or qualification requirements of all applicable state securities Laws. Neither Ibis nor any agent on its behalf has solicited or will solicit any offers to sell or has offered to sell or will offer to sell all or any part of the Additional Shares to any Person or Persons so as to bring the sale of such Additional Shares by Ibis within the registration provisions of the Securities Act or any state securities Laws.

3.2 Representations And Warranties of AMI. AMI hereby represents and warrants to Ibis and Isis as follows (provided that such representations and warranties do not lessen or obviate the representations and warranties of Ibis and Isis set forth in this Agreement):

(a) Power and Authority. AMI has the power, authority and the legal right to enter into this Agreement and to perform its obligations hereunder, and it has taken all

(2) Data for the period reflected in the most recent financial statements available upon exercise of the Subscription Rights will be referenced in this Section.

necessary action required to authorize the execution and delivery of such agreement and the performance of its obligations hereunder.

(b) Enforceability. This Agreement has been duly executed and delivered on behalf of AMI and constitutes its legal, valid and binding obligation and is enforceable against it in accordance with its terms subject to the effects of bankruptcy, insolvency or other Laws of general application affecting the enforcement of creditor rights.

(c) Governmental Authority; Consents. All necessary consents, approvals and authorizations of all Governmental Authorities and other parties required to be obtained by AMI in connection with the execution and delivery of this Agreement and the performance of its obligations hereunder have been obtained.

(d) No Conflicts. The execution and delivery of this Agreement by AMI and the performance of its obligations hereunder and thereunder (i) do not conflict with or violate any requirement of Applicable Law or any provision of its certificate of incorporation or bylaws and (ii) do not require any notice, conflict with, violate, or breach or constitute a default or require any consent not already obtained or give rise to any termination or acceleration right under, any contractual obligation by which such Party is bound.

(e) Due Organization; Qualification. AMI is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, with full corporate power and authority to enter into this Agreement and to perform its obligations hereunder and thereunder.

(f) Investment Representations. AMI understands that the Additional Shares have not been registered under the Securities Act. AMI also understands that the Additional Shares are being offered and sold pursuant to an exemption from registration contained in the Securities Act based in part upon AMI's representations contained in this Agreement. AMI hereby represents and warrants as follows:

(i) *AMI Bears Economic Risk.* AMI may be required to bear the economic risk of its investment in the Additional Shares indefinitely unless the Additional Shares are registered pursuant to the Securities Act, or an exemption from registration is available. AMI understands that Ibis has no present intention of registering the Additional Shares or any shares of its Capital Stock. AMI also understands that there is no assurance that any exemption from registration under the Securities Act will be available and that, even if available, such exemption may not allow AMI to Transfer all or any portion of the Additional Shares under the circumstances, in the amounts or at the times AMI might propose.

(ii) *Acquisition for Own Account.* AMI is acquiring the Additional Shares for AMI's own account for investment only, and not with a view towards their distribution.

(iii) *Accredited Investor.* AMI represents that it is an accredited investor within the meaning of Regulation D under the Securities Act.

(iv) *Ibis Information.* Ibis and Isis have given AMI an opportunity to discuss Ibis' business, management and financial affairs with directors, officers and management of Ibis and AMI has had an opportunity to review Ibis' operations and facilities.

(v) *Rule 144.* AMI acknowledges and agrees that the Additional Shares, are "restricted securities" as defined in Rule 144 promulgated under the Securities Act as in effect from time to time and must be held indefinitely unless they are subsequently registered under the Securities Act or an exemption from such registration is available. AMI has been advised or is aware of the provisions of Rule 144, which permits limited resale of shares purchased in a private placement subject to the satisfaction of certain conditions, including, among other things: the availability of certain current public information about Ibis, the resale occurring following the required holding period under Rule 144 and the number of shares being sold during any three-month period not exceeding specified limitations.

(g) Transfer Restrictions. AMI acknowledges and agrees that the Additional Shares are subject to restrictions on Transfer as set forth in the Investor Rights Agreement.

(h) Legends. AMI understands and agrees that the certificates evidencing the Additional Shares, or any other Capital Stock issued in respect of the Additional Shares upon any stock split, stock dividend, recapitalization, merger, consolidation or similar event, will bear the legends required by the Investor Rights Agreement, including legends relating to restrictions on Transfer under federal and state securities Laws and legends required under applicable state securities Laws.

(i) Master Agreement. AMI has complied with and performed the covenants and agreements set forth in the Investment Documents in all material respects as of the date hereof.

SECTION 4. Indemnification.

4.1 The representations and warranties of Ibis and Isis set forth in Sections 3.1(a), 3.1(b), 3.1(c), 3.1(d), 3.1(e), 3.1(f) and 3.1(g), above and each Fundamental Isis Representation set forth in the Master Agreement as restated on the date hereof shall also be 'Fundamental Isis Representations' under the Master Agreement.

4.2 The representations and warranties of AMI set forth in Sections 3.2(a), 3.2(b), 3.2(c) and 3.2(d), above and each Fundamental AMI Representation set forth in the Master Agreement as restated on the date hereof shall also be 'Fundamental AMI Representations' under the Master Agreement.

4.3 The representations, warranties, covenants and agreements of the Parties set forth in this Agreement shall be subject to Sections 5.8, 7.1 and 7.2 of the Master Agreement.

SECTION 5. Miscellaneous. Section 8 of the Master Agreement is incorporated herein by reference.

[THE REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, the parties hereto have executed this **STOCK SUBSCRIPTION AGREEMENT** as of the date set forth in the first paragraph hereof.

ISIS PHARMACEUTICALS, INC.

Signature: _____

Print Name: _____

Title: _____

Address: _____

_____

IBIS BIOSCIENCES, INC.

Signature: _____

Print Name: _____

Title: _____

Address: _____

_____

ABBOTT MOLECULAR INC.

Signature: _____

Print Name: _____

Title: _____

Address: _____

_____

EXHIBIT C

[***] MILESTONE AND VALUE ACCRETION MILESTONES

[***]

EXHIBIT D

OPTION NOTICE

Reference is made to that certain Call Option Agreement (the "Agreement") dated as of January 30, 2008 by and among Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"), Ibis Biosciences, Inc., a Delaware corporation, and Abbott Molecular Inc., a Delaware corporation ("AMI"). Capitalized terms used but not defined herein have the meanings given to such terms in the Agreement.

AMI hereby notifies Isis that AMI is exercising its Call Option pursuant to the Agreement as of this date of , 200 .

1. The Base Purchase Price, per the Agreement is **[**One Hundred Seventy Five Million and No/100 Dollars ($175,000,000.00)// One Hundred Ninety Five Million and No/100 Dollars ($195,000,000.00)**]**.

2. AMI in its good faith judgment has determined that the [***] Milestone has not been reached as of the date hereof and the Transaction Value is therefore **[**One Hundred Seventy Five Million and No/100 Dollars ($175,000,000.00)// One Hundred Ninety Five Million and No/100 Dollars ($195,000,000.00)**]**.

OR

2. AMI in its good faith judgment has determined that the [***] Milestone has been reached as of the date hereof and:

(i) AMI in its good faith judgment has determined that the [***] Milestone has//has not been reached as of the date hereof;

(ii) AMI in its good faith judgment has determined that the [***] Milestone has//has not been reached as of the date hereof; and

(iii) AMI in its good faith judgment has determined that the [***] Milestone has//has not been reached as of the date hereof and, therefore, the Transaction Value is as follows:

Base Purchase Price	$175,000,000.00// $195,000,000.00	
[[***] Milestone Adjustment	$	[***]]
[[***] Milestone Adjustment	$	[***]]
[[***] Milestone Adjustment]	$	[***]]
Transaction Value	$ [	]

The Transaction Value is $**[ ]**. Pursuant to Section 3.1 of the Agreement, AMI hereby instructs Isis to execute and return the Acquisition Agreement to AMI via facsimile in accordance with the provisions of Section 4.2 of the Agreement upon receipt of this Option Notice.

AMI represents and warrants to Isis that AMI has obtained the consent of its Board of Directors to exercise the Call Option and to execute the Acquisition Agreement based upon the most recent Disclosure Schedules delivered by Isis to AMI.

ABBOTT MOLECULAR INC.

By: _____
Name: _____
Title: _____

EXHIBIT 31.1

CERTIFICATION

I, Stanley T. Crooke, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Isis Pharmaceuticals, Inc.;

2. Based on my knowledge, this quarterly report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this quarterly report;

3. Based on my knowledge, the condensed consolidated financial statements, and other financial information included in this quarterly report, fairly present in all material respects the financial condition, condensed consolidated results of operations and condensed consolidated cash flows of the registrant as of, and for, the periods presented in this quarterly report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: May 12, 2008

/s/ Stanley T. Crooke

Stanley T. Crooke, M.D., Ph.D.
Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, B. Lynne Parshall, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Isis Pharmaceuticals, Inc.;

2. Based on my knowledge, this quarterly report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this quarterly report;

3. Based on my knowledge, the condensed consolidated financial statements, and other financial information included in this quarterly report, fairly present in all material respects the financial condition, condensed consolidated results of operations and condensed consolidated cash flows of the registrant as of, and for, the periods presented in this quarterly report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: May 12, 2008

/s/ B. Lynne Parshall

B. Lynne Parshall, J.D.
Chief Financial Officer

Exhibit 32.1

CERTIFICATION

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Stanley T. Crooke, the Chief Executive Officer of Isis Pharmaceuticals, Inc., (the "Company"), and B. Lynne Parshall, the Chief Financial Officer of the Company, each hereby certifies that, to the best of his or her knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended March 31, 2008, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Periodic Report and the results of operations of the Company for the period covered by the Periodic Report.

Dated: May 12, 2008

/s/ Stanley T. Crooke	/s/ B. Lynne Parshall
Stanley T. Crooke, M.D., Ph.D.	B. Lynne Parshall, J.D.
Chief Executive Officer	Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to Isis Pharmaceuticals, Inc. and will be retained by Isis Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.