SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K/A

(Amendment No.2)

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

Date of report (Date of earliest event reported):

January 30, 2008, amended December 17, 2008, and January 12, 2009

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125 (Commission File No.)

33-0336973

(IRS Employer Identification No.)

1896 Rutherford Road Carlsbad, CA 92008

(Address of Principal Executive Offices and Zip Code)

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

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 1.01. Entry into a Material Definitive Agreement.

On January 30, 2008, Isis Pharmaceuticals, Inc. ("Isis") and its former subsidiary, Ibis Biosciences ("Ibis"), entered into a Strategic Alliance Master Agreement, a Call Option Agreement and an Investor Rights Agreement with Abbott Molecular Inc. ("AMI"), pursuant to which:

- · AMI purchased from Ibis common stock of Ibis representing approximately 10.25% of the issued and outstanding common stock of Ibis for a total purchase price of \$20 million (the "Initial Investment");
- · Ibis granted AMI the right to purchase an additional \$20 million of Ibis common stock before July 31, 2008 (the "Subscription Right"); and
- · Isis granted AMI an exclusive option (the "Call Option") to acquire from Isis all remaining Ibis capital stock.

AMI exercised the Subscription Right and, on June 27, 2008, purchased an additional \$20 million of Ibis common stock (the "Subsequent Investment").

AMI exercised the Call Option and on December 17, 2008, Isis, Ibis and AMI executed a stock purchase agreement (the "Stock Purchase Agreement"). Under the Stock Purchase Agreement, AMI purchased the remaining equity ownership in Ibis from Isis for a closing purchase price of \$175 million. Isis, Ibis and AMI completed the acquisition on January 6, 2009. The Initial Investment and the Subsequent Investment, along with the \$175 million paid by AMI at closing, resulted in a total acquisition price of \$215 million plus the earnout payments described below.

Under the Stock Purchase Agreement, AMI will also pay Isis earn out payments equal to a percentage of Ibis' revenue related to sales of Ibis systems, including instruments, assay kits and successor products from the date of the acquisition closing through December 31, 2025 (the "Earn Out Payments"). The Earn Out Payments will equal 5% of Ibis' cumulative net sales over \$140 million (subject to adjustment) 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. As part of the acquisition, Ibis distributed to Isis, immediately prior to the closing, all cash and cash equivalents held by Ibis as of the closing.

Isis issued a press release in connection with the closing of the acquisition and a copy of the press release is furnished as Exhibit 99.1.

Item 2.01 Completion of Acquisition or Disposition of Assets.

The information set forth in Item 1.01 is incorporated herein by this reference.

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Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

The information set forth in Item 1.01 is incorporated herein by this reference.

As of the closing of the acquisition, Ibis is no longer owned by Isis. As a result, Michael J. Treble and David J. Ecker are no longer employees of Isis, or any of Isis' subsidiaries.

Item 9.01. Financial Statements and Exhibits.

(b) Pro forma financial information.

The unaudited pro forma financial information required by Item 9.01 (b) of Form 8-K, is set forth as Exhibit 99.2 to this report on Form 8-K, which exhibit is hereby incorporated by reference.

- (d) Exhibits.
 - 99.1 Press Release dated January 6, 2009.
 - 99.2 Pro forma financial information

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SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ISIS PHARMACEUTICALS, INC.

Dated: January 7, 2009 By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL Chief Operating Officer,

Chief Financial Officer and Director

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INDEX TO EXHIBITS

99.1 Press Release dated January 6, 2009.

99.2 Pro forma financial information





ABBOTT COMPLETES ACQUISITION OF IBIS BIOSCIENCES, A SUBSIDIARY OF ISIS

CARLSBAD, Calif. and Abbott Park, Ill., January 6, 2009 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) and Abbott (NYSE: ABT) announced today that Abbott has completed its purchase of Ibis Biosciences, Inc., an Isis subsidiary, for a closing purchase price of \$175 million. In addition to the closing purchase price, Isis will receive earn out payments from Abbott tied to post-closing sales of Ibis systems, including instruments and assay kits.

Previously, Abbott invested \$40 million in Ibis in exchange for approximately 18.6% of Ibis' outstanding equity. This investment, along with the \$175 million paid at closing, resulted in a total acquisition price of \$215 million plus earn out payments.

"We believe that Abbott is the ideal company to move the Ibis technology into larger commercial markets, such as clinical diagnostics, where Ibis' technology can revolutionize infectious disease detection," said Stanley Crooke, Chairman and CEO of Isis. "With the earn out, Isis and our shareholders will continue to participate in Ibis' success."

"This acquisition will enable Abbott to offer an innovative approach to the detection and characterization of a broad array of pathogens for the management of infectious diseases," said Stafford O'Kelly, Vice President, Molecular Diagnostics, Abbott. "Ibis' unique technology and talented team of scientists will help us continue building a long-term product pipeline for our growing molecular diagnostics business."

About Abbott Molecular

Abbott's molecular diagnostics business, headquartered in Des Plaines, Ill., provides physicians with critical information based on the early detection of pathogens and key changes in patients' genes and chromosomes, allowing for earlier diagnosis, selection of appropriate therapies and monitoring of disease progression. The business includes instruments and reagents used to conduct sophisticated analysis of patient DNA and RNA.

About Abbott

Abbott is a global, broad-based health care company devoted to the discovery, development, manufacture and marketing of pharmaceuticals and medical products, including nutritionals, devices and diagnostics. The company employs more than 68,000 people and markets its products in more than 130 countries.

Abbott's news releases and other information are available on the company's Web site at www.abbott.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 19 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. 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 1,600 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding Isis Pharmaceuticals' business, the financial position and outlook for Isis, and the commercial potential of Ibis' technologies and products in development. 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, 2007, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

Private Securities Litigation Reform Act of 1995 —A Caution Concerning Forward-Looking Statements

Some statements in this news release may be forward-looking statements for the purposes of the Private Securities Litigation Reform Act of 1995. Abbott cautions that these forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated. Economic, competitive, governmental, technological and other factors that may affect Abbott's operations are discussed in Item 1A, "Risk Factors," to Abbott's Annual Report on Securities and Exchange Commission Form 10-K for the year ended December 31, 2007, and in Item 1A, "Risk Factors," to Abbott's Quarterly Reports on Securities and Exchange Commission Form 10-Q for the quarters ended June 30, 2008, and September 30, 2008, and are incorporated by reference. Abbott undertakes no obligation to release publicly any revisions to forward-looking statements as a result of subsequent events or developments.

In this press release, unless the context requires otherwise, "Isis" and "Company" refers to Isis Pharmaceuticals and its subsidiaries and joint venture.

Isis Pharmaceuticals is a registered trademark of Isis Pharmaceuticals, Inc. Regulus Therapeutics is a trademark of Regulus Therapeutics LLC.

Abbott's Contacts:

Don Braakman Public Affairs, Diagnostics 847-937-0080 or 847-772-3263

Isis Pharmaceuticals' Contacts:

Kristina Lemonidis Associate Director, Corporate Development 760-603-2490 Tina Ventura Director, Investor Relations 847-935-9390

Amy Blackley, Ph.D. Manager, Corporate Communications 760-603-2772

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ISIS PHARMACEUTICALS, INC. INTRODUCTION TO PRO FORMA CONSOLIDATED FINANCIAL INFORMATION

(Unaudited)

On January 30, 2008, Isis Pharmaceuticals, Inc. ("Isis") and its former subsidiary, Ibis Biosciences ("Ibis"), entered into a Strategic Alliance Master Agreement, a Call Option Agreement and an Investor Rights Agreement with Abbott Molecular Inc. ("AMI").

On January 30, 2008, AMI purchased from Ibis common stock of Ibis representing approximately 10.25% of the issued and outstanding common stock of Ibis for a total purchase price of \$20 million (the "Initial Investment"). Ibis also granted AMI the right to purchase an additional \$20 million of Ibis common stock before July 31, 2008 ("Subscription Right"). Additionally, Isis granted AMI an exclusive option (the "Call Option") to acquire from Isis all remaining Ibis capital stock.

On June 27, 2008, AMI exercised the Subscription Right and purchased an additional \$20 million of Ibis common stock (the "Subsequent Investment").

On December 17, 2008, AMI exercised the Call Option and Isis, Ibis and AMI executed a stock purchase agreement (the "Stock Purchase Agreement"). Under the Stock Purchase Agreement, AMI purchased the remaining equity ownership in Ibis from Isis for a closing purchase price of \$175 million. Isis, Ibis and AMI completed the acquisition on January 6, 2009. The Initial Investment and the Subsequent Investment, along with the \$175 million paid by AMI at closing, resulted in a total acquisition price of \$215 million. Prior to the sale of Ibis, Isis identified Ibis as a variable interest entity for which Isis was the primary beneficiary. Therefore, Isis' historical consolidated financial statements leading up to the completion of the sale on January 6, 2009 include the financial position and results of operations of Ibis.

The accompanying unaudited pro forma consolidated statements of operations for the years ended December 31, 2005, 2006 and 2007 and the nine months ended September 30, 2008, give effect to the disposition of Ibis as if it had been consummated at the beginning of the periods presented. The accompanying unaudited pro forma condensed consolidated balance sheet as of September 30, 2008 gives effect to the disposition of Ibis as if it had been consummated as of September 30, 2008.

The historical financial information on which the pro forma statements are based is included in Isis' Annual Report on Form 10-K for the fiscal year ended December 31, 2007, which was filed on March 13, 2008, and Isis' Quarterly Report on Form 10-Q for the quarter ended September 30, 2008, which was filed on November 10, 2008. The pro forma consolidated financial statements and the notes thereto should be read in conjunction with these historical consolidated financial statements.

The unaudited pro forma consolidated financial statements are presented for illustrative purposes only and are subject to a number of assumptions which may not be indicative of the results of operations that would have occurred had the disposition been completed at the dates indicated or what the results will be for any future periods. The unaudited pro forma consolidated statements of operations do not include the gain that Isis would have recognized for the sale of Ibis if the transaction was completed at the beginning of the periods presented.

ISIS PHARMACEUTICALS, INC. PRO FORMA CONDENSED CONSOLIDATED BALANCE SHEET (in thousands) (Unaudited)

Ph	armaceuticals, Inc.	Pro Forma Adjustments		Notes		Pro Forma ptember 30, 2008
\$	264,682	\$	168,933	1	\$	433,615
	247,341		_			247,341
	5,021		(53)	2		4,968
	5,511		(3,034)	2		2,477
	6,988		(273)	2		6,715
	529,543		165,573			695,116
	14,019		(1,914)	2		12,105
	17,447		_			17,447
	18,126		(1,845)	2		16,281
	5,557		(81)	2		5,476
\$	584,692	\$	161,733		\$	746,425
\$	6,885	\$	(2,080)	2	\$	4,805
	3,956		(373)	2		3,583
	5,979		(1,866)	2		4,113
	1,069		(1,069)	2		_
	\$ \$	\$ 264,682 247,341 5,021 5,511 6,988 529,543 14,019 17,447 18,126 5,557 \$ 584,692 \$ 6,885 3,956 5,979	\$ 264,682 \$ 247,341	Pharmaceuticals, Inc. Inc. September 30, 2008 Pro Forma Adjustments \$ 264,682 \$ 168,933 247,341 — 5,021 (53) 5,511 (3,034) 6,988 (273) 529,543 165,573 14,019 (1,914) 17,447 — 18,126 (1,845) 5,557 (81) \$ 584,692 \$ 161,733 \$ 6,885 \$ (2,080) 3,956 (373) 5,979 (1,866)	Pharmaceuticals, Inc. September 30, 2008 Pro Forma Adjustments Notes \$ 264,682 \$ 168,933 1 247,341 — — 5,021 (53) 2 5,511 (3,034) 2 6,988 (273) 2 529,543 165,573 14,019 (1,914) 2 17,447 — — 18,126 (1,845) 2 5,557 (81) 2 \$ 584,692 \$ 161,733 \$ 6,885 \$ (2,080) 2 3,956 (373) 2 5,979 (1,866) 2	Pharmaceuticals, Inc. September 30, 2008 Pro Forma Adjustments Notes Section \$ 264,682 \$ 168,933 1 \$ 247,341 —

99,794

117,683

(712)

(6,100)

2

Current portion of deferred contract revenue

Total current liabilities

162,500	_			162,500
5,478	_			5,478
191,279	(69)	2		191,210
476,940	(6,169)			470,771
6,315	_			6,315
33,359	(33,359)	3		_
96	_			96
900,303	_			900,303
(1,271)	_			(1,271)
(831,050)	201,261	4		(629,789)
68,078	201,261			269,339
\$ 584,692	\$ 161,733		\$	746,425
	5,478 191,279 476,940 6,315 33,359 96 900,303 (1,271) (831,050) 68,078	5,478 — 191,279 (69) 476,940 (6,169) 6,315 — 33,359 (33,359) 96 — 900,303 — (1,271) — (831,050) 201,261 68,078 201,261	5,478 — 191,279 (69) 2 476,940 (6,169) 6,315 — 33,359 (33,359) 3 96 — 900,303 — (1,271) — (831,050) 201,261 4 68,078 201,261	5,478 — 191,279 (69) 476,940 (6,169) 6,315 — 33,359 (33,359) 3 — 96 — 900,303 — (1,271) — (831,050) 201,261 4 68,078 201,261

Note 1: This adjustment is recorded to reflect net cash that Isis estimates it would have received as consideration for the sale of Ibis if the transaction was completed on September 30, 2008.

Note 2: These adjustments are recorded to reflect the disposition of Ibis' assets and liabilities as of September 30, 2008.

Note 3: This adjustment is recorded to remove the noncontrolling interest in Ibis that was recognized on the historical balance sheet as a result of the consolidation of Ibis as a variable interest entity.

Note 4: This amount represents the estimated gain on the sale of Ibis and consists of the following adjustments:

- Upon the closing of the transaction, Isis received \$175 million, but was required, concurrent with the closing, to pay off approximately \$4.7 million in liabilities.
- · The removal of Ibis' net assets of \$2.4 million and the non-controlling interest of \$33.4 million on the balance sheet as of September 30, 2008

ISIS PHARMACEUTICALS, INC. PRO FORMA CONSOLIDATED STATEMENT OF OPERATIONS (in thousands, except for per share amounts) (Unaudited)

Revenue: 28,610 \$ (11,793) 1 \$ 16,817 Licensing and royalty revenue 11,523 — 11,523 Total revenue 40,133 (11,793) 28,340 Expenses: — 82,467 (12,931) 1 69,536 Selling, general and administrative 8,432 (1,090) 1 7,342 Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 5,094 — 5,094 Investment income 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)			Historical Isis Pharmaceuticals, Inc. Year Ended December 31, 2005		Pro Forma Adjustments	Notes		Pro Forma Year Ended December 31, 2005
Licensing and royalty revenue 11,523 — 11,523 Total revenue 40,133 (11,793) 28,340 Expenses: — (12,931) 1 69,536 Research and development 8,432 (1,090) 1 7,342 Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): — 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)		_			====		_	
Total revenue 40,133 (11,793) 28,340 Expenses: 82,467 (12,931) 1 69,536 Selling, general and administrative 8,432 (1,090) 1 7,342 Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 5,094 — 5,094 Investment income 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)		\$		\$	(11,793)	1	\$	
Expenses: Research and development 82,467 (12,931) 1 69,536 Selling, general and administrative 8,432 (1,090) 1 7,342 Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 1 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Licensing and royalty revenue		11,523		<u> </u>		_	11,523
Expenses: Research and development 82,467 (12,931) 1 69,536 Selling, general and administrative 8,432 (1,090) 1 7,342 Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 1 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)								
Research and development 82,467 (12,931) 1 69,536 Selling, general and administrative 8,432 (1,090) 1 7,342 Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 1 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)			40,133	_	(11,793)		_	28,340
Selling, general and administrative 8,432 (1,090) 1 7,342 Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)								
Compensation benefit related to variable accounting of stock options (544) — (544) Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expenses): 5,094 — 5,094 Investment income 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)	•							
Restructuring activities 6,960 — 6,960 Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 1 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)			8,432		(1,090)	1		7,342
Total operating expenses 97,315 (14,021) 83,294 Loss from operations (57,182) 2,228 (54,954) Other income (expense): 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)			(544)		_			(544)
Loss from operations (57,182) 2,228 (54,954) Other income (expense): 5,094 — 5,094 Investment income 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Restructuring activities		6,960		<u> </u>			6,960
Loss from operations (57,182) 2,228 (54,954) Other income (expense): 5,094 — 5,094 Investment income 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)								
Other income (expense): 1 Investment income 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Total operating expenses		97,315		(14,021)			83,294
Investment income 5,094 — 5,094 Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Loss from operations		(57,182)		2,228		' <u></u>	(54,954)
Interest expense (20,313) — (20,313) Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Other income (expense):							
Net loss from continuing operations \$ (72,401) \$ 2,228 \$ (70,173) Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Investment income		5,094		_			5,094
Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Interest expense		(20,313)		_			(20,313)
Basic and diluted net loss per share \$ (1.15) \$ (1.12)								
Basic and diluted net loss per share \$ (1.15) \$ (1.12)	Net loss from continuing operations	\$	(72,401)	\$	2,228		\$	(70,173)
	· .			_	<u> </u>		_	
	Basic and diluted net loss per share	\$	(1.15)				\$	(1.12)
Shares used in computing basic and diluted net loss per share 62,877 62,877								
	Shares used in computing basic and diluted net loss per share		62,877					62,877

Note 1: These adjustments are recorded to remove Ibis' revenue and operating expenses from Isis' results from continuing operations.

		Historical Isis Pharmaceuticals, Inc. Year Ended December 31, 2006 Adjustments Notes			Pro Forma Year Ended December 31, 2006	
Revenue:						
Research and development revenue under collaborative agreements	\$	15,091	\$	(9,673)	1	\$ 5,418
Licensing and royalty revenue		9,441		_		9,441
Total revenue		24,532		(9,673)		14,859
Expenses:						
Research and development		80,567		(13,674)	1	66,893
Selling, general and administrative		12,619		(2,939)	1	9,680
Restructuring activities		(536)		· _		(536)
-						
Total operating expenses		92,650		(16,613)		76,037
Loss from operations		(68,118)		6,940		 (61,178)
Other income (expense):						
Investment income		5,960		_		5,960
Interest expense		(9,029)		_		(9,029)
Gain on investments, net		2,263		_		2,263
Loss attributed to noncontrolling interest in Symphony GenIsis, Inc.		23,021		_		23,021
		<u>, </u>				 <u> </u>
Net loss from continuing operations	\$	(45,903)	\$	6,940		\$ (38,963)
	_		_	<u> </u>		
Basic and diluted net loss per share	\$	(0.62)				\$ (0.52)
	_					
Shares used in computing basic and diluted net loss per share		74,308				74,308

Note 1: These adjustments are recorded to remove Ibis' revenue and operating expenses from Isis' results from continuing operations.

ISIS PHARMACEUTICALS, INC. PRO FORMA CONSOLIDATED STATEMENT OF OPERATIONS (in thousands, except for per share amounts) (Unaudited)

		Historical Isis Pharmaceuticals, Inc. Year Ended December 31, 2007	Pro Forma Adjustments Notes			1	Pro Forma Year Ended Occember 31, 2007
Revenue:	ф	22.500	ф	(44.055)	4	ф	22.240
Research and development revenue under collaborative agreements	\$	33,596	\$	(11,277)	1	\$	22,319
Licensing and royalty revenue	_	36,025	_				36,025
Total revenue		69,621		(11,277)			58,344
Expenses:		<u> </u>	_				<u>, </u>
Research and development		92,641		(17,164)	1		75,477
Selling, general and administrative		15,928		(4,918)	1		11,010
						<u></u>	
Total operating expenses		108,569		(22,082)			86,487
Loss from operations		(38,948)		10,805		<u></u>	(28,143)
Other income (expense):							
Investment income		11,443		_			11,443
Interest expense		(7,573)		_			(7,573)
Gain on investments		3,510		_			3,510
Loss on early retirement of debt		(3,212)		_			(3,212)
Loss attributed to noncontrolling interest in Symphony GenIsis, Inc.		23,157		_			23,157
Loss attributed to noncontrolling interest in Regulus Therapeutics							
LLC		629		_			629
Net loss from continuing operations		(10,994)		10,805			(189)
Basic and diluted net loss per share	\$	(0.13)				\$	(0.00)
Shares used in computing basic and diluted net loss per share	_	83,739					83,739

Note 1: These adjustments are recorded to remove Ibis' revenue and operating expenses from Isis' results from continuing operations.

PRO FORMA CONDENSED CONSOLIDATED STATEMENT OF OPERATIONS (in thousands, except for per share amounts) (Unaudited)

	Historical Isis Pharmaceuticals, Inc. Nine Months Ended September 30, 2008		Pro Forma Adjustments		Notes	Nine I	ro Forma Months Ended otember 30, 2008
Revenue:							
Research and development revenue under collaborative agreements	\$	78,739	\$	(8,989)	1	\$	69,750
Licensing and royalty revenue		7,790		<u> </u>			7,790
Total revenue		86,529		(8,989)			77,540
Expenses:							
Research and development		89,611	(18,539)	1		71,072
Selling, general and administrative		13,206		(5,193)	1		8,013
Total operating expenses		102,817	(2	23,732)			79,085
Loss from operations		(16,288)		14,743			(1,545)
Other income (expense):							
Investment income		13,061		(4,257)	2		8,804
Interest expense		(4,297)		_			(4,297)
Loss attributed to noncontrolling interest in Regulus Therapeutics LLC		3,056					3,056
Loss attributed to noncontrolling interest in Ibis Biosciences, Inc.		1,163		(1,163)	3		
Net income (loss) from continuing operations	\$	(3,305)	\$	9,323		\$	6,018
Basic and diluted net income (loss) per share	\$	(0.04)				\$	0.06
Shares used in computing basic net income (loss) per share		93,786					93,786
		23,700					33,730
Shares used in computing diluted net income (loss) per share		93,786					98,508

Note 1: These adjustments are recorded to remove Ibis' revenue and operating expenses from Isis' results from continuing operations.

Note 2: This adjustment is recorded to remove the non-cash adjustments related to the value of the call option and subscription right that Isis granted to Abbott.

Note 3: This adjustment is recorded to remove the loss attributed to noncontrolling interest in Ibis that was recognized on Isis' historical statement of operations as a result of the consolidation of Ibis as a variable interest entity.