SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

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

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))
- o 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 subsidiary, Ibis Biosciences ("IB"), 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 IB common stock of IB representing approximately 10.25% of the issued and outstanding common stock of IB for a total purchase price of \$20 million (the "Initial Investment");
- IB granted AMI the right to purchase an additional \$20 million of IB common stock before July 31, 2008, which when combined with the Initial Investment would represent approximately 18.6% of the issued and outstanding common stock of IB (the "Subscription Right");
- · Isis granted AMI an exclusive option (the "Call Option") to acquire from Isis (the "Final Acquisition") all remaining IB capital stock not acquired pursuant to the Initial Investment or the Subscription Right for a purchase price of \$175 million (which, subject to the satisfaction of certain conditions, may be increased to as much as \$190 million) (the "Base Purchase Price") and earn-out payments as described below. The parties have also agreed that, in the event the Final Acquisition is consummated, IB may distribute to Isis, immediately prior to the closing, all cash on hand at IB and any receivables or other payments due to IB under government contracts and grants held by IB as of the closing; and
- In the event the Final Acquisition is consummated, AMI will also pay Isis earn out payments equal to a percentage of IB's revenue related to sales of IB systems, including instruments, assay kits and successor products from the date of the Final Acquisition closing through December 31, 2025 (the "Earn Out Payments"). The Earn Out Payments will equal 5% of IB's cumulative net sales over \$150 million (subject to adjustment) and up to \$2.1 billion, and 3% of IB's 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.

Terms of Strategic Alliance Master Agreement

The Strategic Alliance Master Agreement (the "SAM Agreement") provides for the Initial Investment and the Subscription Right and, in connection with the Initial Investment, it further provides that AMI, Isis and IB will enter into the Call Option Agreement and the Investor Rights Agreement. The SAM Agreement contains standard representations and warranties and affirmative and negative covenants. Prior to the earlier of the expiration of the Call Option or the Final Acquisition, Isis and IB must obtain AMI's consent before Isis or IB can take specified actions, such as amending IB's certificate of

2

Terms of the Call Option Agreement

The exclusive Call Option Agreement provides that AMI may elect to exercise the Call Option and consummate the Final Acquisition pursuant to the terms of a definitive Stock Purchase Agreement (the "SPA"). The SPA would be executed by the parties upon the exercise of the Call Option. The Call Option initially expires on December 31, 2008, provided that, subject to certain conditions, AMI may extend the term of the Call Option through June 30, 2009. In addition, if AMI does not exercise its Subscription Right by July 31, 2008, the Call Option will expire.

If AMI exercises the Call Option, the closing of the Final Acquisition would be subject to the terms of the SPA. The Final Acquisition is subject to the premerger notification provisions of the Hart-Scott-Rodino Antitrust Improvements Act.

Terms of the Investor Rights Agreement.

In connection with the Initial Investment, Isis, IB and AMI entered into an Investor Rights Agreement (the "IRA"). The IRA includes demand and piggybank registration rights, tag-along rights, participation rights and a make whole provision. Under the make whole provision, in the event of a liquidation or change of control of Ibis, AMI will receive a payment equal to the price paid per share of the capital stock of IB acquired by AMI in the Initial Investment or under the Subscription Right, plus a yield of 3% annually from the date AMI purchases the IB common stock, prior to the distribution of any proceeds to any other holders of IB capital stock. Thereafter, the other holders of IB capital stock will receive an amount per share of IB capital stock equal to the amount per share received by AMI with respect to its shares. Thereafter, any remaining proceeds will be paid equally on a per share basis to all holders of IB capital stock.

Isis issued a press release in connection with entering into the Strategic Alliance Master Agreement, the Call Option Agreement and the Investor Rights Agreement and a copy of the press release is furnished as Exhibit 99.1.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated January 31, 2008.

3

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 30, 2008 By: /s/ B. Lynne Parshall

B. LYNNE PARSHALLChief Operating Officer,

Chief Financial Officer and Director

4

INDEX TO EXHIBITS

99.1 Press Release dated January 31, 2008.



Isis Pharmaceuticals' Contacts:

Kristina Lemonidis Associate Director, Investor Relations 760-603-2490 Amy Blackley, Ph.D. Manager, Corporate Communications 760-603-2772

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., January 31, 2008 –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™ 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™ 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

1

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 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™ 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 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.

Isis Pharmaceuticals is a registered trademark of Isis Pharmaceuticals, Inc. Ibis Biosciences and Ibis T5000 are trademarks of Ibis Biosciences, Inc. Regulus Therapeutics is a trademark of Regulus Therapeutics LLC.

###