

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K/A

(Amendment No.1)

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**

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 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 (the "Subscription Right"); and
- Isis granted AMI an exclusive option (the "Call Option") to acquire from Isis all remaining IB capital stock.

AMI exercised the Subscription Right and, on June 27, 2008, purchased an additional \$20 million of IB common stock (the "Subsequent Investment"), which when combined with the Initial Investment represents approximately 18.6% of the issued and outstanding common stock of IB.

AMI exercised the Call Option and, on December 17, 2008, Isis, IB and AMI entered into a stock purchase agreement providing for AMI's purchase of the remaining equity ownership in Ibis from Isis for a closing purchase price of \$175 million (the "Stock Purchase Agreement"). The Initial Investment and the Subsequent Investment, along with the \$175 million that will be due at closing, would result in a total acquisition price of \$215 million plus the earnout payments described below.

The closing of the acquisition of the remaining equity ownership in Ibis is subject to the satisfaction of the terms and conditions set forth in the Stock Purchase Agreement, including obtaining clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976.

In the event the 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 acquisition closing through December 31, 2025 (the "Earn Out

Payments”). The Earn Out Payments will equal 5% of IB’s cumulative net sales over \$140 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. The parties have also agreed that, in the event the 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.

Isis issued a press release in connection with AMI’s exercise of the Call Option and a copy of the press release is furnished as Exhibit 99.1.

This report includes forward-looking statements regarding Isis Pharmaceuticals’ business, the financial position and outlook for Isis as well as its Ibis Biosciences subsidiary 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.

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Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated December 17, 2008.

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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: December 17, 2008

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL
Chief Operating Officer,
Chief Financial Officer and Director

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99.1 Press Release dated December 17, 2008.

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**ABBOTT EXERCISES ITS OPTION TO ACQUIRE IBIS BIOSCIENCES,
A SUBSIDIARY OF ISIS**

**Total acquisition price will be \$215 million
Acquisition will expand Abbott's position in molecular diagnostics for infectious disease**

CARLSBAD, Calif. and Abbott Park, Ill., December 17, 2008 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) and Abbott (NYSE: ABT) announced today that Abbott has exercised its option to purchase the remaining equity ownership in 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.

Earlier this year, Abbott invested \$40 million in Ibis in exchange for approximately 18.6% of Ibis' outstanding equity. This investment, along with the \$175 million that would be due at closing, would result in a total acquisition price of \$215 million plus earn out payments.

The closing of the acquisition of the remaining equity ownership in Ibis is subject to the satisfaction of the terms and conditions of a stock purchase agreement that has been executed by the parties, including obtaining clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, and is expected to occur in January, 2009.

"Abbott's confidence in Ibis is reflected in its decision to invest in Ibis' technology and to exercise its option to purchase Ibis. We have already presented development plans for the next-generation instrument that will facilitate our rapid growth into clinical diagnostics," said Michael Treble, President of Ibis. "This year we have made substantial progress by advancing our broad pathogen detection and characterization capabilities and establishing a foundation for our commercial clinical diagnostic products. We look forward to continuing this progress."

"The broad applicability of Ibis' technology has been demonstrated in biodefense applications, microbial forensics and infectious disease detection and surveillance, and we believe that it has the potential to be a powerful tool in the detection and surveillance of infectious diseases in the hospital and clinical settings," added Stafford O'Kelly, Vice President, Molecular Diagnostics, Abbott.

"Ibis is an example of Isis' broad innovation, and will provide substantial benefit to our shareholders, both now as well as in the future, as Isis receives earn out payments associated with sales of Ibis products," said Stanley Crooke, M.D., Ph.D., Chairman and CEO of Isis. "Ibis has refined its approach toward larger commercial markets, and we believe its relationship with Abbott will allow Ibis to continue to move quickly forward along this path."

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 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. Additional information about Ibis can be found by selecting the Ibis link from Isis' homepage at www.isispharm.com.

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 1,500 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 as well as its Ibis Biosciences subsidiary 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. Ibis Biosciences and Ibis T5000 are trademarks of Ibis Biosciences, Inc. Regulus Therapeutics is a trademark of Regulus Therapeutics LLC.

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