
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): **April 8, 2013**

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.)

**2855 Gazelle Court
Carlsbad, CA 92010**

(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))
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Item 1.01. Entry into a Material Definitive Agreement.

On April 8, 2013, Isis Pharmaceuticals, Inc. ("**Isis**") and Roche announced that they have formed an alliance to develop treatments for Huntington's disease (HD) based on Isis' antisense oligonucleotide (ASO) technology.

Isis and Roche filed a press release describing this transaction. A copy of this press release is attached as Exhibit 99.1 to this Current Report and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated April 8, 2013.

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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: April 8, 2013

By: /s/ B. Lynne Parshall

INDEX TO EXHIBITS

99.1 Press Release dated April 8, 2013.



Basel, Switzerland and Carlsbad, CA, USA — 08 April, 2013

Roche and Isis Pharmaceuticals form alliance for Huntington's disease

Roche (SIX: RO, ROG; OTCQX: RHHBY) and Isis Pharmaceuticals, Inc (NASDAQ: ISIS) today announced that they have formed an alliance to develop treatments for Huntington's disease (HD) based on Isis' antisense oligonucleotide (ASO) technology. This alliance combines Isis' antisense expertise with Roche's scientific expertise in developing neurodegenerative therapeutics. In addition, Isis and Roche will be collaborating to combine Isis' ASOs and Roche's proprietary "brain shuttle" program with the objective of increasing the brain penetration of ASOs with systemic administration.

Huntington's disease is an inherited genetic brain disorder that results in the progressive loss of both mental faculties and physical control. Symptoms usually appear between the ages of 30 to 50, and worsen over a 10 to 25 year period. Ultimately, the weakened individual succumbs to pneumonia, heart failure or other complications. Presently, there is no effective treatment or cure for the disease, and current treatments focus on reducing the severity of some disease symptoms.

Initially, research will focus on Isis' lead drug candidate that blocks production of all forms of the huntingtin (HTT) protein, the protein responsible for HD and thus has the potential to treat all HD patients. Isis is also conducting research into treatments that specifically block production of the disease-causing forms of the HTT protein which has the potential to treat subsets of HD patients. In parallel, Roche will combine its proprietary brain shuttle technology with Isis ASO technology that, if successful, will also allow systemic administration of antisense drugs to treat asymptomatic patients.

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Under the terms of the agreement, Roche will make an upfront payment of \$30 million to Isis, with total payments related to license fee and pre- and post-licensing milestone payments reaching potentially \$362 million, including up to \$80 million in potential commercial milestone payments. In addition, Isis will receive tiered royalties on sales of the drugs. Roche has the option to license the drugs from Isis through the completion of the first Phase 1 trial. Prior to option exercise, Isis is responsible for the discovery and development of an antisense drug targeting HTT protein. Roche and Isis will work collaboratively on the discovery of an antisense drug utilizing Roche's "brain shuttle" program. If Roche exercises its option, it will be responsible for global development regulatory and commercialization activities for all drugs arising out of the collaboration.

Commenting on the deal, Luca Santarelli, Head of Neuroscience and Small Molecules Research at Roche, said: "Huntington's is a severely debilitating neurodegenerative disease and a large unmet medical need. Patients experience gradually worsening motor function and psychological disturbances, with a significant shortening of life expectancy after the disease is diagnosed. Treatments are urgently needed, and we believe that the Isis approach in combination with Roche's brain shuttle represent one of the most advanced programs targeting the cause of HD with the aim of slowing down or halting the progression of this disease."

Shafique Virani, Global Head Neuroscience, Cardiovascular & Metabolism at Roche Partnering, added: "Central to the partnership is Roche's brain shuttle program, which we see as highly complementary to Isis' drug development work. This dual track development program ensures whichever candidate compound proves to be most promising — Isis' lead target or Roche's brain shuttle version — can be taken forward to pivotal clinical trials."

"We are pleased to be working with Roche, a global leader in drug development with significant experience in developing and commercializing drugs to treat neurological diseases. We believe that Roche's expertise in developing CNS drugs, along with their clinical development experience, will greatly enhance our development efforts for this program and allow us to move forward more rapidly. In addition, by utilizing Roche's brain shuttle technology with our antisense drug discovery capabilities, we have the

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potential to significantly improve the therapeutic potential for this program," said B. Lynne Parshall, Chief Operating Officer of Isis. "By partnering our more complex and nuanced research and development programs earlier in development, like our Huntington's disease CNS program, we add value and resources with partners that bring unique benefits."

"We are excited to be working with Roche," said Frank Bennett, Senior Vice President of Research at Isis. "We believe our mature antisense drug discovery platform is a perfect fit for Roche's neuroscience franchise, and we anticipate a fruitful collaboration to advance our pre-clinical compounds."

CHDI Foundation, a non-profit foundation exclusively dedicated to the development of therapies that slow the progression of HD, provided financial and scientific support to Isis' HD drug discovery program through a development collaboration with Isis. CHDI's support has enabled Isis to make significant progress in discovering a drug to treat HD. Together Isis and CHDI demonstrated that antisense compounds can be used to inhibit the production of HTT protein in both brain and peripheral tissues, and that the inhibition of normal HTT protein was well tolerated. Over time, CHDI will be reimbursed for its support of Isis' program out of the milestone payments received by Isis. CHDI will receive \$1.5 million associated with the signing of the Roche agreement. CHDI will continue to provide advice to Isis and Roche on the development of antisense drugs to treat patients with HD.

Isis also recognizes the tremendous benefit provided to its HD program by its academic collaborators, Drs. Don Cleveland at the Ludwig Institute, University of California San Diego and David Corey at University of Texas Southwestern. These collaborators have been instrumental in Isis' early preclinical work demonstrating that antisense drugs can inhibit the HTT protein and produce activity in animal models of disease.

Conference Call

At 9:45 a.m. Eastern Time today, April 08, 2013, Isis will conduct a live webcast conference call to discuss the alliance with Roche. Interested parties may listen to the call by dialing 866-323-2841 and provide the conference identification number "34237203", or access the webcast at www.isispharm.com. A webcast replay will be available for a limited time at the same address.

About Isis Pharmaceuticals, Inc.

Isis is exploiting its leadership position in antisense technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 28 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO™, in the United States for the treatment of patients with HoFH. Genzyme is also pursuing marketing approval of KYNAMRO in other markets. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at www.isispharm.com.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, infectious diseases, inflammation, metabolism and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2012 Roche had over 82,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 45.5 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

All trademarks used or mentioned in this release are protected by law.

About Roche Neurosciences

Roche is working on new molecular entities in neuroscience that could become the next generation of medicines for a range of diseases including schizophrenia, multiple sclerosis, depression, neurodevelopmental disorders, Parkinson's disease and Alzheimer's disease. With one of the strongest neuroscience pipelines in the industry, and by working closely with academic institutions, biotech companies, and forming public-private partnerships, Roche's focus is on expanding its neuroscience franchise to better serve patients.

Isis Pharmaceuticals' Forward-Looking Statement

This press release includes forward-looking statements regarding Isis' strategic alliance with Roche, Isis' research and development opportunities in neurological diseases, the development, activity and therapeutic potential of an antisense drug targeting the huntingtin gene to treat Huntington's disease. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of KYNAMRO, is a forward-looking statement and should be considered an at-risk statement. 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, and in the endeavor of building a business around such drugs. 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, 2012, which is on file with the SEC. Copies of this and other documents are available from the Company.

Isis Pharmaceuticals® is a registered trademark of Isis Pharmaceuticals, Inc. KYNAMRO™ is a trademark of Genzyme Corporation.

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