

# 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): **December 2, 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 December 2, 2009, Isis Pharmaceuticals, Inc. ("Isis") and Eli Lilly and Company ("Lilly") entered a Drug Development and License Option Agreement, pursuant to which Isis reacquired from Lilly the rights to ISIS-EIF4E<sub>Rx</sub>, an antisense drug formerly known as LY2275796 that was discovered by Isis and licensed to Lilly for the treatment of cancer. Isis recently announced that it is reinvigorating its internal cancer program, and ISIS-EIF4E<sub>Rx</sub> will be the first drug in development under this new initiative. Isis will independently develop ISIS-EIF4E<sub>Rx</sub> for the treatment of multiple types of cancer, including, potentially, breast, lung, prostate, bladder and colon cancers. A Phase 1 study in patients with cancer has been completed with ISIS-EIF4E<sub>Rx</sub>.

ISIS-EIF4E<sub>Rx</sub> targets eukaryotic initiation factor-4E (eIF-4E), a protein involved in the translation of key growth and survival factors that contribute to tumor progression and the spread of cancer. In 2006, Isis and collaborators published data that provided the first *in vivo* evidence that cancers may be more susceptible to eIF-4E inhibition than normal tissues.

Isis will be responsible for clinical development of ISIS-EIF4E<sub>Rx</sub> going forward. Lilly will have the right to reacquire ISIS-EIF4E<sub>Rx</sub> on predefined terms prior to the initiation of Phase 3 development. Lilly will continue to develop LY2181308, another antisense drug discovered by Isis and licensed to Eli Lilly and Company for the treatment of cancer that is currently in Phase 2 development.

This report includes forward-looking statements regarding the development, activity, therapeutic potential and safety of ISIS-EIF4E<sub>Rx</sub> in the treatment of cancer. 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. 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 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, 2008, 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 Isis.

**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 7, 2009

By: /s/ B. Lynne Parshall

**B. LYNNE PARSHALL**

Chief Operating Officer,

Chief Financial Officer and Director