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): October 31, 2022

IONIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

000-19125	**33-0336973**
(Commission File No.)	(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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol	Name of each exchange on which registered
Common Stock, $.001 Par Value	"IONS"	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (Section 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (Section 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 1.02 Termination of a Material Definitive Agreement.

On November 4, 2022, Ionis Pharmaceuticals, Inc. (the "***Company***") issued a press release announcing that while fesomersen, an investigational antisense therapy that is being evaluated to reduce the production of Factor XI for the prevention of thrombosis, achieved its primary endpoint in the Phase 2b RE-THINC ESRD study, the Company's partner, Bayer AG ("***Bayer***"), is discontinuing the Bayer-led clinical development program for fesomersen and will return development and commercialization rights to fesomersen to the Company.

A copy of this press release is attached as Exhibit 99.1 to this Current Report and incorporated herein by reference.

The Company entered into a License Agreement with Bayer for the development and commercialization of fesomersen on May 1, 2015 (the "***License Agreement***"), as amended on February 10, 2017 ("***Amendment #1***") (collectively, the "***Agreement***"). Under the terms of the Agreement, the Company granted Bayer an exclusive license, with the right to grant certain sublicenses, to research, develop, manufacture and commercialize fesomersen worldwide. The Agreement will terminate effective January 29, 2023.

The foregoing description of the Agreement is a summary only and is qualified in its entirety by reference to the terms of the License Agreement and Amendment #1, copies of each of which were filed as Exhibit 10.50 and 10.11, respectively, to the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	**Description**
99.1	Press Release dated November 4, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

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.

IONIS PHARMACEUTICALS, INC.

Dated: November 4, 2022

By: /s/ Patrick R. O'Neil

PATRICK R. O'NEIL
Executive Vice President, Chief Legal Officer and General Counsel

Exhibit 99.1

Ionis announces positive results from fesomersen development program

- *Positive Phase 2b data from RE-THINC ESRD study of fesomersen in patients on hemodialysis presented at Kidney Week 2022*
- *Ionis to regain rights to fesomersen from Bayer*

CARLSBAD, Calif., November 4, 2022 – Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced positive results from the Phase 2b RE-THINC ESRD study of fesomersen (formerly IONIS-FXI-L_{Rx}), an investigational antisense medicine designed to reduce the production of Factor XI (FXI) for the prevention of thrombosis, were presented by Bayer at the American Society of Nephrology's (ASN) Kidney Week 2022. The RE-THINC ESRD study evaluated fesomersen in patients with end-stage renal disease (ESRD) on hemodialysis.

In the study, fesomersen achieved its primary endpoint, demonstrating no increase in the incidence of the composite of major bleeding and clinically relevant non-major (CRNM) bleeding with 24 weeks of treatment. Fesomersen also achieved dose-dependent and sustained median reductions in steady-state FXI levels of 53.1%, 72.2% and 86.6% in the 40 mg, 80 mg, and 120 mg doses of fesomersen, respectively, administered once every 4 weeks. statistically significant. Incidences of dialysis circuit clotting and AV-access thrombosis diminished significantly with decreasing FXI levels, both of which were exploratory efficacy endpoints. Fesomersen showed favorable safety and tolerability with 48 weeks of treatment in this study.

"We are very pleased with the efficacy and safety data seen in the Phase 2b study of fesomersen in patients with ESRD, which we believe supports continued advancement of this potential novel anti-thrombotic therapy for patients with renal and cardiovascular diseases," said Richard S. Geary, Ph.D., executive vice president and chief development officer at Ionis. "We thank Bayer for their partnership in the development of fesomersen. We are focused on getting fesomersen into the hands of a new partner to deliver it to the market and patients in need."

About the RE-THINC ESRD Study

RE-THINC ESRD (NCT04534114) is a randomized, double-blind, placebo-controlled study evaluating the safety, pharmacokinetics and pharmacodynamics of multiple doses of fesomersen in 307 patients with end-stage renal disease on hemodialysis. Study participants were randomized to each of 3 dose cohorts or placebo administered subcutaneously every four weeks for up to 48 weeks. The RE-THINC ESRD study was conducted by Bayer, which licensed fesomersen from Ionis.

About Thrombosis

Thrombosis is the formation of blood clots inside blood vessels. Blood clots can obstruct blood flow to prevent sufficient oxygen flow to tissues and organs. In addition, clot fragments can break off from the blood clot and travel to occlude other parts of the circulation. Thrombosis is responsible for many heart attacks and strokes and is the leading cause of morbidity and mortality worldwide. Current anti-thrombotic treatments include anticoagulants such as warfarin, Factor Xa inhibitors and thrombin inhibitors. Although these therapies are effective at lowering the risk of thrombosis, they can place patients at significant risk of bleeding because they target factors required for normal coagulation.

About Fesomersen

Fesomersen, (formerly IONIS-FXI-L_{Rx}) is an investigational antisense medicine designed by Ionis to reduce the production of Factor XI, a clotting factor produced in the liver that is an important component of the coagulation pathway. High levels of Factor XI increase the risk of blood clot formation inside blood vessels (thrombosis), which can cause heart attacks and strokes. Alternatively, individuals deficient in Factor XI have a lower incidence of thrombosis-related events and little to no increase in bleeding risk. This makes Factor XI an attractive target for an anti-thrombotic medicine because of the potential to separate anti-thrombotic activity from bleeding risk. Although currently available anticoagulants reduce the risk of thrombosis, these anticoagulants are associated with increased bleeding risk at therapeutic doses, which can lead to major, sometimes fatal, bleeding events.

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry-leading cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming a leading, fully integrated biotechnology company.

To learn more about Ionis, visit www.ionispharma.com and follow us on Twitter @ionispharma.

Ionis' Forward-looking Statements

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of Ionis' technologies, fesomersen and other products in development. Any statement describing Ionis' 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, including those related to the impact COVID-19 could have on our business, and including but not limited to, those related to our commercial products and the medicines in our pipeline, and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Ionis' 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 Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on Form 10-K for the year ended December 31, 2021, and the most recent Form 10-Q quarterly filing, which are on file with the Securities and Exchange Commission. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals and its subsidiaries.

Ionis Pharmaceuticals Investor Contact:
760-603-2331

Ionis Pharmaceuticals Media Contact:
760-603-4679

# # #