Ionis Pharmaceuticals Reports Positive Phase 2 Data for IONIS-FXI Rx in Patients with End-Stage Renal Disease on Hemodialysis

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-- Statistically significant, dose-dependent reductions in Factor XI activity observed --

CARLSBAD, Calif., Nov. 1, 2016 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced positive data from a Phase 2 placebo-controlled study evaluating IONIS-FXI$_{Rx}$ in patients with end-stage renal disease (ESRD) on hemodialysis. In this Phase 2 study patients treated with IONIS-FXI$_{Rx}$ achieved statistically significant, dose-dependent reductions in Factor XI activity. There were no clinically meaningful reductions in platelet levels and no treatment-related major or clinically relevant non-major bleeding events.

"IONIS-FXI$_{Rx}$ is the first and only antithrombotic in development to have demonstrated potential to separate antithrombotic activity from bleeding risk. In this Phase 2 study in patients with ESRD on hemodialysis, it was important to evaluate the safety profile of IONIS-FXI$_{Rx}$ in these patients who are at high-risk for bleeding. These new data are consistent with those of our previous Phase 2 comparator-controlled study evaluating the incidence of venous thromboembolic events (VTE) in patients treated with IONIS-FXI$_{Rx}$ undergoing total knee replacement surgery. In that Phase 2 study, patients treated with 300 mg IONIS-FXI$_{Rx}$ had a 7-fold lower incidence of VTE with no increase in bleeding events compared with patients treated with enoxaparin," said Sanjay Bhanot, M.D., Ph.D., vice president of development at Ionis.

The Phase 2 study of IONIS-FXI$_{Rx}$ was a double-blinded, randomized, placebo-controlled study in 43 patients with ESRD receiving hemodialysis. The primary purpose of the study was to understand the drug's behavior and activity in patients with severe kidney disease on dialysis. Patients received 200 mg or 300 mg of IONIS-FXI$_{Rx}$ or placebo for 12 weeks. In patients treated with 200 mg and 300 mg of IONIS-FXI$_{Rx}$, a mean percent reduction in FXI activity of 56% (p=<0.001) and 71% (p=<0.001), respectively, was achieved at week 13, compared to a mean percent reduction of 4% for placebo-treated patients. Furthermore, a decrease in severe clotting events in the dialysis circuit after six weeks compared to baseline was observed. IONIS-FXI$_{Rx}$ displayed a favorable safety and tolerability profile. In this small 3-month study, there were no clinically meaningful reductions in platelets and no treatment-related major or clinically relevant non-major bleeding events. There were no treatment-related serious adverse events. An increase in minor bleeding events was observed in patients receiving the 300 mg dose. In addition, there were no clinically meaningful changes in laboratory values, including those related to liver function. IONIS-FXI$_{Rx}$ was well tolerated in the study with no flu-like or injection site reactions.

"IONIS-FXI$_{Rx}$ is a prime example of the power of antisense technology to selectively target a key component of the complex antithrombotic pathway that is not easy to target with other therapeutic modalities," said Richard Geary, Ph.D., senior vice president of development at Ionis. "Patients with ESRD are at high risk of thrombotic and bleeding events and have defective platelet function. Therefore, to see such a good safety profile in this study gives us additional confidence that antisense drugs might be safely used in patients with severe kidney disease. We were also encouraged by the absence of clinically meaningful platelet declines in this study. Even though this was a small 3-month study, it provided further evidence that 2'MOE antisense oligonucleotides, as a class, are not associated with clinically meaningful platelet declines."

In May 2015, Ionis entered into an exclusive license agreement with Bayer to develop and commercialize IONIS-FXI$_{Rx}$ for the prevention of clotting disorders. Upon review of the Phase 2 data and potential advancement of the program by Bayer, Ionis will be eligible to receive a $55 million payment.

ABOUT IONIS PHARMACEUTICALS, INC.

Ionis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Ionis has created a large pipeline of first-in-class or best-in-class drugs, with over a dozen drugs in mid- to late-stage development. Drugs currently in Phase 3 development include volanesorsen, a drug Ionis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy; IONIS-TTR$_{Rx}$, a drug Ionis is developing with GSK to treat patients with TTR amyloidosis; and SPINRAZA (nusinersen), a drug Ionis is developing with Biogen to treat infants and children with spinal muscular atrophy. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

IONIS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Ionis' alliance with Bayer, the development, activity, therapeutic and commercial potential and safety of IONIS-FXI$_{Rx}$. 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, 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. 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, 2015, 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.

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

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