



Ionis' License Agreement for Huntington's Disease Drug, IONIS-HTT Rx, Receives HSR Clearance

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Ionis Earns \$45 Million License Fee

CARLSBAD, Calif., Dec. 18, 2017 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced today that its license agreement with Roche to develop and commercialize IONIS-HTT_{Rx} for the treatment of people with

Huntington's disease (HD) has received clearance under the Hart-Scott-Rodino Antitrust Improvements Act. Based on Roche's decision to license the drug and this approval, Ionis has earned a \$45 million license fee from Roche. Roche is now responsible for all IONIS-HTT_{Rx} development, regulatory and commercialization activities and costs. The two companies will work together to transition the ongoing open-label extension study to Roche, which will be responsible for managing this study and all future studies.



ABOUT IONIS-HTT_{Rx} and HUNTINGTON'S DISEASE (HD)

IONIS-HTT_{Rx} is an antisense drug in development for the treatment of HD. IONIS-HTT_{Rx} is designed to reduce the production of all forms of the huntingtin (HTT) protein, which in its mutated variant (mHTT) is responsible for HD. As such, IONIS-HTT_{Rx} offers a unique approach to treat all patients with HD, irrespective of their individual HTT mutation. IONIS-HTT_{Rx} has been granted orphan drug designation by the U.S. Food and Drug Administration (FDA) and by the European Medicines Agency (EMA) for the treatment of patients with HD.

HD is a rare, genetic, progressive, neurodegenerative disease resulting in deterioration in mental abilities and physical control. In the U.S., there are approximately 30,000 individuals with symptomatic HD and more than 200,000 people at risk of having inherited HD. HD is referred to as a triplet repeat disorder and is one of a large family of genetic diseases in which certain gene sequences are mistakenly repeated. In HD, the trinucleotide sequence in the gene that encodes for the HTT protein is repeated more than 36 times. The resulting mHTT protein is toxic and gradually damages neurons in the brain. Symptoms of HD usually appear between the ages of 30 to 50 years and continually 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 disease-modifying treatment for HD, and current products focus only on managing disease symptoms.

ABOUT IONIS/ROCHE COLLABORATION

Roche and Ionis are collaborating to develop antisense drugs to treat HD. The alliance combines Ionis' antisense expertise with Roche's knowledge in clinical development of anti-neurodegenerative therapeutics. In total, Ionis has generated \$100 million in up-front, milestone and license payments and is eligible to receive an additional \$275 million in milestone payments as the drug progresses in development. In addition, Ionis is eligible to receive tiered double-digit royalties up to the mid-teens on sales of IONIS-HTT_{Rx} if it is commercialized.

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 three dozen drugs in development. SPINRAZA[®] (nusinersen) has been approved in global markets for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs that have successfully completed Phase 3 studies include inotersen, an antisense drug Ionis is developing to treat patients with hereditary TTR amyloidosis (hATTR), and volanesorsen, an antisense drug discovered by Ionis and co-developed by Ionis and Akcea Therapeutics to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy. Akcea, an affiliate of Ionis, is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders. If approved, volanesorsen will be commercialized through Ionis' affiliate, Akcea. Inotersen filings for marketing approval have been submitted in the U.S. and EU. Volanesorsen filings for marketing approval have been submitted in the U.S., EU, and Canada. 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 Roche and the development, activity, therapeutic potential, commercial potential and safety of IONIS-HTT_{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, 2016, 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.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics™ is a trademark of Ionis Pharmaceuticals, Inc. SPINRAZA® is a registered trademark of Biogen.

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