

Ionis Enters New Collaboration with Partner to Develop IONIS-FB-L Rx for Complement-Mediated Diseases

October 10, 2018

**Transaction valued at up to \$760 million, including \$75 million upfront payment, plus royalties up to 20%
Planned Phase 2 program to begin in early 2019**

CARLSBAD, Calif., Oct. 10, 2018 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today announced a new collaboration with Roche to develop IONIS-FB-L_{Rx} for the treatment of complement-mediated diseases. This collaboration will leverage Ionis' leadership in RNA-targeted therapeutics to develop IONIS-FB-L_{Rx} targeting Factor B (FB) for a broad range of diseases. The first indication the two companies will pursue is the treatment of patients with Geographic Atrophy (GA), the advanced stage of dry age-related macular degeneration (AMD). A Phase 2 study in patients with GA is planned to begin in early 2019.



"Ionis is committed to bringing new therapies to patients living with unmet medical needs. The collaboration is designed to maximize both the potential benefit to patients and the likelihood of success, while optimizing our commercial participation in IONIS-FB-L_{Rx}. This new agreement builds upon our productive relationship with Roche on IONIS-HTT_{Rx} (RG6042), an antisense drug for the treatment of people with Huntington's disease," said Brett P. Monia, chief operating officer at Ionis. "Our antisense technology is the first to demonstrate robust, dose-dependent and sustained reduction of FB in a clinical study. We believe that we have found the right partner whose experience in retinal disease drug development and commercialization will enhance our efforts to effectively develop IONIS-FB-L_{Rx} for patients who currently have no adequate treatment options."

IONIS-FB-L_{Rx}, an antisense drug using Ionis' advanced **Ligand Conjugated Antisense (LICA)** technology, reduces the production of FB, a key protein in the complement innate immune system. FB is predominately produced in the liver and circulates throughout the vascular system, including vessels in the eye and kidney. This complement protein plays a pivotal role in an innate immunogenic cascade that, when overactivated, has been associated with the development of several complement-mediated diseases, including dry AMD.

In a Phase 1 study in 54 healthy volunteers IONIS-FB-L_{Rx} reduced plasma FB and was safe and well tolerated.

Under this new collaboration with Roche, Ionis will receive a \$75 million upfront payment. In addition, Ionis is eligible to receive up to \$684 million in development, regulatory and sales milestone payments and license fees. Ionis also has the potential to receive tiered royalties that range from the high teens to twenty percent on sales from the product when commercialized. Ionis is responsible for conducting a Phase 2 study in patients with dry AMD and exploring the drug in a rare severe renal indication. Roche has the option to license IONIS-FB-L_{Rx} at the completion of the studies. Upon licensing, Roche will be responsible for all global development and commercialization activities.

About AMD

Age-related macular degeneration, or AMD is the most common cause of blindness in the elderly population that can progress through a succession of stages from early to late. Late stages of AMD are classified as "wet" or "dry," with approximately 90 percent of U.S. cases diagnosed as "dry." Dry AMD is the leading cause of blindness in the U.S. and developed countries. This disease is expected to affect up to 3 million people in the U.S. and 196 million people worldwide by 2020.¹ Geographic Atrophy (GA) is a late stage manifestation of dry AMD resulting from a progressive loss of retinal pigment epithelial (RPE) cells, photoreceptor cells and choriocapillaries in the central retina. Patients with GA experience trouble with facial recognition, decreased reading speeds and difficulty driving at night, and ultimately, blindness.² It is estimated that more than 5 million people worldwide suffer from GA, a disease with no approved therapies.³

About Ionis Pharmaceuticals, Inc.

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, proprietary antisense technology platform with the potential to treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs – such as children and adults with spinal muscular atrophy (SMA). We created SPINRAZA[®] (nusinersen)* and are proud to have brought new hope to the SMA community by developing the first and only approved treatment for this disease.

Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 drugs with the potential to treat patients with cardiovascular disease, rare diseases, neurological diseases, infectious diseases and cancer. We created TEGSEDI[™] (inotersen) the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy of hereditary transthyretin (TTR) amyloidosis (ATTR) in adult patients that our affiliate Akcea Therapeutics is commercializing. Together with Akcea, we are also bringing new medicines to patients with cardiometabolic lipid disorders.

To learn more about Ionis follow us on twitter @ionispharma or visit <http://ir.ionispharma.com/>.

*Spinraza is marketed by Biogen.

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} (RG6042) and IONIS-FB-L_{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, 2017, and its most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of this 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 Akcea Therapeutics, Inc. TEGSEDI [™] is a trademark of Akcea Therapeutics, Inc. WAYLIVRA [™] is a trademark of Akcea Therapeutics, Inc. SPINRAZA[®] is a registered trademark of Biogen.

References

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