Ionis' partner provides update on clinical studies evaluating tominersen (IONIS-HTT Rx)

March 22, 2021

- Dosing to stop in Phase III clinical study of tominersen and paused in the open-label extension study (GEN-EXTEND)
- The Phase I PK/PD study (GEN-PEAK) of tominersen and the observational Roche HD Natural History Study will continue
- No new or emerging safety signals for tominersen were identified
- Ionis to host webcast today, March 22, 2021, at 5 p.m. ET

CARLSBAD, Calif., March 22, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced its partner, Roche, has decided to discontinue dosing in the Phase III GENERATION HD1 study of tominersen in manifest Huntington's disease (HD). The decision was based on the results of a pre-planned review of data from the Phase III study conducted by an unblinded Independent Data Monitoring Committee (iDMC). While there were no new or emerging safety signals identified for tominersen, the iDMC made its recommendation based on the investigational therapy's potential benefit/risk profile for study participants. Participants will continue to be followed for safety and clinical outcomes.

"We are very disappointed by this news," said Brett Monia, Ph.D., Ionis CEO. "This of course is not the outcome we have been working towards or hoped for, as we have grown quite close to the HD patient community over the years. We are committed to finding treatments for this devastating disease and want to thank the patients, their families and the entire HD community for their partnership, trust and dedication. We look forward to learning more once Roche has evaluated the full data."

In addition, dosing will be paused in the open-label extension study (GEN-EXTEND) of tominersen while data are carefully analyzed to inform next steps on this study. Roche also stated that the Phase I PK/PD study (GEN-PEAK) of tominersen and Roche's observational HD Natural History Study will continue.

Roche has stated that once full data from the studies are available and analyzed, Roche will share learnings and future plans with the community.

About tominersen and the clinical trials

Tominersen, previously IONIS-HTT_{Rx} or RG6042, is an investigational antisense therapy designed to reduce the production of all forms of the huntingtin protein (HTT), including its mutated variant, mHTT. In December 2017, Roche licensed the investigational molecule from Ionis.

Tominersen is being investigated in Huntington's disease in the following clinical studies:

- GENERATION HD1: a randomized, multicenter, double-blind, placebo-controlled Phase III clinical study evaluating the efficacy and safety of treatment with tominersen in people with manifest HD over 25 months. Study participants were randomized to either 120 mg every two months or 120 mg every four months intrathecal injections of tominersen, or placebo. The study has recruited 791 participants from 18 countries around the world.
- GEN-EXTEND: an open label extension study for participants coming from any Roche HD study. Participants receive 120 mg tominersen every two months or every four months in the study.
- GEN-PEAK: a Phase I study aiming to better understand the pharmacokinetics of tominersen and how tominersen affects mHTT levels and other markers in the spinal fluid and blood, which studies a range of doses from 30 mg to 120 mg of tominersen over two administrations.

About Huntington's disease

Huntington's disease is a rare genetic, progressive condition that causes the nerve cells in the brain to break down, causing problems with a person's ability to think, move and function, leading to increasing disability and loss of independence. It has a devastating impact on people living with the disease, and the hereditary nature of HD means it profoundly affects entire families for generations. Survival ranges from approximately 10-20 years following motor onset of the disease. There is no known cure for HD and no approved therapies that treat the underlying cause.

Ionis will hold a webcast on Monday, March 22, 5 p.m. ET to discuss this update. Visit www.ionispharma.com for more information and to register.

About Ionis' Neurology Franchise

The Ionis neurology franchise addresses all major brain regions and central nervous system types, currently has three Phase 3 studies, eight medicines in clinical development and five are wholly owned. Ionis is leading the way in treating the root causes of many neurological diseases and developing antisense medicines for common diseases like Alzheimer's and Parkinson's, rare diseases like ALS, Huntington's disease, and Alexander disease. Ionis' marketed neurological disease medicines include SPINRAZA®, the global foundation of care for spinal muscular atrophy (SMA), commercialized by Biogen, and TEGSEDI®, the first and only self-administered, subcutaneous treatment for the polyneuropathy of hereditary ATTR amyloidosis in adults.

About Ionis Pharmaceuticals

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 neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

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

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business, Ionis' technologies, tominersen, 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, 2020, which is 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.

View original content to download multimedia:http://www.prnewswire.com/news-releases/ionis-partner-provides-update-on-clinical-studies-evaluating-tominersen-ionis-htt-rx-301253134.html

SOURCE Ionis Pharmaceuticals, Inc.

Ionis Pharmaceuticals Investor Contact: D. Wade Walke, Ph.D., Vice President, Investor Relations, 760-603-2741; Ionis Pharmaceuticals Media Contact: Roslyn Patterson, Vice President, Marketing and Communications , 760-603-4679