Ionis announces positive donidalorsen late-stage clinical progress in HAE

June 1, 2023

- *Two-year treatment with donidalorsen in the Phase 2 open label study resulted in consistent, sustained protection from HAE attacks*
- *Completed enrollment in the Phase 3 OASIS-HAE study*
- *Topline Phase 3 results expected in H1 2024*

CARLSBAD, Calif., June 1, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced positive clinical progress with donidalorsen, its late-stage investigational prophylactic therapy for hereditary angioedema (HAE). Topline two-year open-label extension (OLE) results continue to demonstrate consistent efficacy and safety, with an overall sustained mean reduction in HAE attack rates of 96% from baseline through two years across dosing groups. The company also announced that it has completed enrollment in the Phase 3 OASIS-HAE study, which is evaluating the safety and efficacy of donidalorsen in preventing angioedema attacks. Topline data from the study are expected in the first half of 2024. HAE is a rare and potentially fatal genetic disease characterized by severe and potentially fatal swelling of the arms, legs, face and throat[1,2].

"By completing enrollment in the Phase 3 study, we are one step closer to bringing a potentially transformative and differentiated prophylactic treatment to HAE patients," said Richard S. Geary, Ph.D., executive vice president and chief development officer at Ionis. "We are also encouraged by the long-term safety and durable efficacy results seen in patients treated for two years in our ongoing open-label extension study. We look forward to the Phase 3 data readout in the first half of 2024 and are advancing our go-to-market preparations to commercialize donidalorsen."

The two-year Phase 2 OLE results will be presented at an upcoming medical congress.

In the Phase 2 study, through week 17, donidalorsen 80 mg monthly demonstrated a 90% reduction in angioedema attacks compared with placebo after the first dose, and a 97% reduction in angioedema attacks starting with the second dose. The Phase 2 results also showed a significant improvement in quality of life as assessed by the Angioedema Quality of Life Questionnaire (AE-QoL), in the patients treated with donidalorsen. Donidalorsen continues to demonstrate a favorable safety and tolerability profile with added two-year OLE data.

About OASIS-HAE

OASIS-HAE is a multi-center, double-blind, randomized, placebo-controlled study of monthly and bimonthly subcutaneous injections of donidalorsen or placebo in 84 participants, age 12 and above, with Type 1 and Type 2 hereditary angioedema (HAE). The study is designed to evaluate the safety and efficacy of donidalorsen in participants with HAE and the effect of donidalorsen on the severity and pattern of HAE attacks and its impact on quality of life (QoL). Participants were randomized in a 2:1 ratio to Cohort A (donidalorsen or placebo every four weeks) or Cohort B (donidalorsen or placebo every eight weeks), respectively. Within each cohort, participants were randomized in a 3:1 ratio to receive donidalorsen or matching-placebo. The primary endpoint is the time-normalized number of investigator-confirmed HAE attacks from week one to 25. A key secondary endpoint is change in the Angioedema Quality of Life Questionnaire (AE-QoL) total score at week 25. Additional information about OASIS-HAE (NCT05139810) and the Phase 2 open-label extension study (NCT04307381) may be found at ClinicalTrials.gov.

About Hereditary Angioedema (HAE)

HAE is a rare and potentially fatal genetic disease characterized by severe and potentially fatal swelling of the arms, legs, face and throat1,2. HAE is estimated to affect more than 20,000 patients in the U.S. and Europe. In the U.S., doctors frequently use prophylactic treatment approaches to prevent and reduce the severity of HAE attacks in patients.

About Donidalorsen

Donidalorsen is an investigational **LI**gand-**C**onjugated **A**ntisense (LICA) medicine designed to target the prekallikrein, or PKK, pathway. PKK plays an important role in the activation of inflammatory mediators associated with acute attacks of hereditary angioedema (HAE). By inhibiting the production of PKK, donidalorsen could be an effective prophylactic approach to preventing HAE attacks.

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been a leader in RNA-targeted therapy, pioneering new markets and changing standards of care with its novel antisense technology. Ionis currently has four marketed medicines and a promising late-stage pipeline highlighted by cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision to become the leader in genetic medicine, utilizing a multi-platform approach to discover, develop and deliver life-transforming therapies.

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 donidalorsen, Ionis' technologies 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 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 Dec. 31, 2022, 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" all refer to Ionis Pharmaceuticals and its subsidiaries.

Ionis Pharmaceuticals® is a registered trademark of Ionis Pharmaceuticals, Inc.

[1] Cicardi M, et al. Allergy. 2012;67(2): 147-157.
[2] Zuraw BL. N Engl J Med. 2008;359(10): 1027-1036.

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