Ionis announces positive topline results from Phase 3 OASIS-HAE study of investigational donidalorsen in patients with hereditary angioedema

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- *Donidalorsen met the primary endpoint with a statistically significant reduction in the rate of HAE attacks in patients treated every 4 weeks or patients treated every 8 weeks*
- *Donidalorsen demonstrated a favorable safety and tolerability profile*
- *Ionis is preparing to submit a New Drug Application with U.S. FDA*
- *Data to be presented at an upcoming medical congress*

CARLSBAD, Calif., Jan. 22, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced positive topline results for the Phase 3 OASIS-HAE study of donidalorsen in people with hereditary angioedema (HAE). The trial met its primary endpoint of reduction in rate of angioedema attacks in patients treated with donidalorsen (80mg) via subcutaneous injection dosed every 4 weeks (Q4W) ($p<0.001$) or every 8 weeks (Q8W) ($p=0.004$), compared to placebo. In addition, the trial showed donidalorsen achieved statistical significance on all secondary endpoints in the Q4W group and key secondary endpoints in the Q8W group. Donidalorsen demonstrated a favorable safety and tolerability profile in the study, and there were no serious adverse events in the patients treated with donidalorsen.

HAE is a rare and life-threatening genetic disease that causes unpredictable and frequent severe swelling of the skin, gastrointestinal (GI) tract, upper respiratory system, face and throat. Donidalorsen is an investigational RNA-targeted prophylactic medicine designed to precisely target and silence the production of prekallikrein (PKK), interrupting the pathway that leads to HAE attacks.

Based on these data, Ionis is preparing to submit a New Drug Application with the U.S. Food and Drug Administration. Otsuka, which has exclusive rights to commercialize donidalorsen in Europe, is preparing to submit a Marketing Authorization Application to the European Medicines Agency. Donidalorsen received Orphan Drug Designation in the U.S., and the Orphan Drug Designation procedure in the EU is ongoing.

"We are very pleased with the positive topline results from the Phase 3 OASIS-HAE study of donidalorsen," said Kenneth Newman, M.D., senior vice president, head of clinical development at Ionis. "Based on these results and the durable efficacy and favorable safety data seen in the ongoing Phase 2 open-label extension study, we believe donidalorsen, if approved, could be an attractive new treatment option for patients with HAE, many of whom continue to experience unpredictable, painful and severe breakthrough attacks despite currently available prophylactic treatments. We are grateful to the patients, caregivers, investigators and study teams who participated in the OASIS-HAE study."

"These data represent our third highly positive Phase 3 readout over the last 12 months, underscoring the strength of our LICA platform for RNA-targeted medicines," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "Following the recent launch of WAINUA™ (eplontersen), we are now well on our way to independently launching medicines from our wholly owned pipeline with regulatory submissions this year for olezarsen in familial chylomicronemia syndrome and donidalorsen in HAE. These achievements, coupled with our robust R&D pipeline, position Ionis to continue to deliver a steady cadence of potentially transformational medicines to people with serious diseases for years to come."

Ionis plans to present the Phase 3 OASIS-HAE results at an upcoming medical congress by mid-year. Ionis also plans to share results from the Phase 3 OASIS-Plus study by mid-year, which includes both the open-label extension of the Phase 3 trial and a separate cohort of patients who have transitioned to donidalorsen from another prophylactic HAE medication (switch cohort).

About the OASIS-HAE Study

The global, multicenter, randomized, double-blind, placebo-controlled Phase 3 OASIS-HAE study (NCT05139810) enrolled 91 participants, age 12 and above, with Type 1 and Type 2 hereditary angioedema (HAE). Participants were randomized in a 2:1 ratio to receive donidalorsen 80 mg or placebo via subcutaneous injection once every four weeks for 24 weeks or donidalorsen 80 mg or placebo via subcutaneous injection once every eight weeks for 24 weeks. Within each cohort, participants were randomized in a 3:1 ratio to receive donidalorsen or matching-placebo. The primary endpoint was the time-normalized number of investigator-confirmed HAE attacks from week one to week 25 compared to placebo. More than 90% of patients completed the OASIS-HAE study. Following completion of the treatment period, over 90% of randomized patients entered the Phase 3 OASIS-Plus open-label extension study.

About the OASIS-Plus Study

The Phase 3 OASIS-Plus open-label extension (OLE) study is a 53-week global, multicenter study of subcutaneous injections of donidalorsen administered every four weeks (80mg) and every eight weeks (80mg) in patients completing the OASIS-HAE trial. These are patients aged 12 and above, with Type 1 and Type 2 hereditary angioedema (HAE). The study is designed to evaluate the safety and efficacy of extended dosing of donidalorsen following completion of the Phase 3 OASIS-HAE study. The OASIS-Plus switch cohort is evaluating the safety and efficacy of long-term dosing of donidalorsen every four weeks in patients who were previously treated with another prophylactic HAE medication. Additional information

about OASIS-Plus (NCT04307381) may be found at ClinicalTrials.gov.

About Hereditary Angioedema (HAE)

HAE is a rare and life-threatening genetic disease characterized by unpredictable and frequently severe swelling of the skin, gastrointestinal (GI) tract, upper respiratory system, face, and throat, which can be life-threatening[1,2,3,4,5]. HAE is estimated to affect more than 20,000 people in the U.S. and Europe[6]. 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 RNA investigational **LI**gand-**C**onjugated **A**ntisense (LICA) medicine designed to precisely target and silence the production of prekallikrein (PKK), interrupting the pathway that leads to HAE attacks. PKK plays an important role in activating inflammatory mediators associated with acute attacks of hereditary angioedema (HAE). By silencing the production of PKK, donidalorsen could be an effective prophylactic approach to treating HAE.

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. Ionis currently has five 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 X (Twitter) @ionispharma and LinkedIn.

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.

[1] Manning ME. Dermatol Ther (Heidelb). 2021; 11:1829-1838.
[2] Valerieva A, et al. Balkan Med J. 2021;8:89-103.
[3] Santacroce R, et al. J Clin Med. 2021;10:2023.
[4] Pines JM, et al. J Emerg Med. 2021;60:35-43.X
[5] Maurer M, et al. World Allergy Organ J. 2022;15:100627.
[6] Weller K, et al. Allergy. 2016;71(8): 1203-1209.

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