Ionis presents positive two-year results from the Phase 2 open label extension study of donidalorsen in patients with hereditary angioedema

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- *Continued treatment over two years with donidalorsen demonstrated sustained reduction in hereditary angioedema attacks and improved quality of life*
- *Donidalorsen recently received orphan drug designation in the U.S.*
- *Topline Phase 3 results expected in H1 2024*

CARLSBAD, Calif., Nov. 9, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced positive results from an ongoing Phase 2 open-label extension (OLE) study evaluating the safety and efficacy of its investigational prophylactic medicine, donidalorsen, in patients with hereditary angioedema (HAE), a rare and life-threatening genetic disease. Over the two years, patients treated with donidalorsen via subcutaneous injection showed an overall sustained mean reduction in HAE attack rates of 96% from baseline, from 2.70 to 0.06 attacks per month, across all dosing groups. Furthermore, all patients treated with donidalorsen reported a clinically meaningful improvement in quality of life as measured by the Angioedema Quality of Life Questionnaire (AE-QoL) over two years. Treatment with donidalorsen was well tolerated in the studies, and there were no serious adverse events.

"Hereditary angioedema is a significant healthcare challenge for which there is an ongoing need for long-term, sustained prophylactic treatment offering patients significant efficacy and tolerability that is easy to use," said Richard S. Geary, Ph.D., executive vice president and chief development officer at Ionis. "We are very encouraged by the demonstrated safety, efficacy, and quality of life profile of donidalorsen. The two-year OLE results further support donidalorsen as a potentially compelling prophylactic treatment option for patients with hereditary angioedema. We look forward to reporting pivotal topline Phase 3 results in the first half of next year."

Following the 13-week blinded, placebo-controlled Phase 2 study, patients were eligible for enrollment in the OLE study. Of the 20 Phase 2 study participants, 17 entered the OLE study and were on a fixed 13-week dosing period where they received donidalorsen 80 mg every four weeks. From week 17 through two years, patients entered a flexible dosing period where they either received donidalorsen 80 mg every four weeks, 80 mg every eight weeks, or 100 mg every four weeks.

In a subset analysis also presented at the American College of Allergy, Asthma & Immunology (ACAAI) Annual Scientific Meeting, 62.5% of patients receiving donidalorsen 80 mg every eight weeks remained attack-free over the two-year period and had a sustained mean reduction in HAE attack rates of 83% from baseline.

Injection site (IS) discoloration and IS reaction were the only study drug-related treatment-emergent adverse events (TEAEs) reported in more than one patient (n=2, 11.8% each). No serious adverse events were reported in the OLE study, and no TEAEs led to study discontinuation.

The poster presentations about the Phase 2 Open-Label Extension Study and the sub-analysis of the eight-week dosing arm are available on the ACAAI website.

About Phase 2 Open-Label Extension Study

- An open-label extension study of donidalorsen in up to 24 participants, age 18 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 administered subcutaneously (SC), with 80 mg every four- or eight weeks and 100 mg every four weeks.
- Additional information about the Phase 2 open-label extension study (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[1-5].
- HAE is estimated to affect more than 20,000 patients 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 investigational **LI**gand-**C**onjugated **A**ntisense (LICA) medicine designed to target the prekallikrein, or PKK, pathway.
- PKK plays an important role in activating inflammatory mediators associated with acute attacks of hereditary angioedema (HAE).
- To reduce 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. 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 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 Dec. 31, 2022, and most recent Form 10-Q, which are on file with the SEC. Copies of these and other documents are available at www.ionispharma.com.

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SOURCE Ionis Pharmaceuticals, Inc.

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