DAWNZERA™ (donidalorsen) approved in the U.S. as first and only RNA-targeted prophylactic treatment for hereditary angioedema

- *DAWNZERA demonstrated significant and sustained HAE attack rate reduction and long-term disease control –*
- *Offers longest dosing option for HAE, with dosing every 4 or 8 weeks –*
- *Compelling profile supported by recently published switch data –*
- *Ionis' second independent launch in just nine months, with potential for two additional launches next year –*
- *Ionis to host webcast today at 12:15pm ET –*

CARLSBAD, Calif., Aug. 21, 2025 /Business Newswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced today that the U.S. Food and Drug Administration (FDA) has approved DAWNZERA™ (donidalorsen) for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older. DAWNZERA is the first and only RNA-targeted medicine approved for HAE, designed to target plasma prekallikrein (PKK), a key protein that activates inflammatory mediators associated with acute attacks of HAE. DAWNZERA 80mg is self-administered via subcutaneous autoinjector once every four (Q4W) or eight weeks (Q8W).

HAE is a rare and potentially life-threatening genetic condition that involves recurrent attacks of severe swelling (angioedema) in various parts of the body, including the hands, feet, genitals, stomach, face and/or throat. HAE is estimated to affect approximately 7,000 people in the U.S.

"DAWNZERA represents a significant advance for people living with HAE who need improved treatment options. With strong and durable efficacy, convenient administration and the longest dosing option available, we believe DAWNZERA will be the prophylactic treatment of choice for many people living with HAE. Importantly, the recently published switch data empowers patients and physicians with a roadmap for switching to DAWNZERA from other prophylactic therapies," said Brett P. Monia, Ph.D., chief executive officer, Ionis. "At Ionis, we are dedicated to turning groundbreaking science into life-changing medicines. With the early success of our first independent launch of TRYNGOLZA® for familial chylomicronemia syndrome (FCS), and now with DAWNZERA, our second independent medicine approved in less than nine months, we are proudly delivering on that vision. To the patients, families, advocacy partners and investigators who helped make this moment a reality, we express our deepest gratitude."

The approval of DAWNZERA was based on positive results from the Phase 3 global, multicenter, randomized, double-blind, placebo-controlled OASIS-HAE study in patients with HAE. The study met its primary endpoint, with DAWNZERA Q4W significantly reducing monthly HAE attack rate by 81% compared to placebo over 24 weeks. Mean attack rate reduction increased to 87% when measured from the second dose, a key secondary endpoint. Additionally, DAWNZERA Q4W reduced moderate-to-severe HAE attacks by ~90% over 24 weeks when measured from the second dose.

These results are bolstered by the ongoing OASISplus open-label extension (OLE) study, in which DAWNZERA Q8W had a similar effect as Q4W over time. DAWNZERA demonstrated 94% total mean attack rate reduction from baseline across both dosing groups after one year in the OLE.

The OASISplus study also includes a switch cohort evaluating DAWNZERA Q4W in patients previously treated with lanadelumab, C1-esterase inhibitor or berotralstat for at least 12 weeks. Switching to DAWNZERA reduced mean HAE attack rate by 62% from prior prophylactic treatment over 16 weeks, with no mean increase in breakthrough attacks observed during the switch. A total of 84% of patients surveyed preferred DAWNZERA over their prior prophylactic treatment, citing better disease control, less time to administer and less injection site pain or reactions.

Across clinical studies, DAWNZERA demonstrated a favorable safety and tolerability profile. The most common adverse reactions (incidence ≥ 5%) were injection site reactions, upper respiratory tract infection, urinary tract infection and abdominal discomfort.

“As the first FDA-approved RNA-targeted therapy for HAE, DAWNZERA represents a welcome advance in therapeutic options for preventing attacks. Today’s approval gives people living with HAE and their physicians another important choice for aligning treatment with individual needs,” said Anthony J. Castaldo, CEO & chairman of the board, U.S. Hereditary Angioedema Association (HAEA) and Hereditary Angioedema International (HAEi).

"People living with HAE manage this condition for all their lives, and many continue to face unpredictable, painful and dangerous breakthrough attacks even with current treatments. Durable efficacy is essential in maintaining long-term disease control,” said Marc Riedl, M.D., M.S., clinical director, U.S. HAEA Angioedema Center; University of California, San Diego; OASIS-HAE and OASISplus trial investigator. "DAWNZERA is positioned to help meet patient needs, providing substantial and sustained reduction of HAE attacks, continued improvement over time and reduced burden of treatment.”

DAWNZERA will be available in the U.S. in the coming days.

Ionis is committed to helping people access the medicines they are prescribed and will offer a suite of services designed to meet the unique needs of the HAE community through Ionis Every Step™. As part of Ionis Every Step, patients and healthcare providers will have access to a wide range of support and resources including dedicated support from a Patient Education Manager, assistance with the insurance approval process, information on affordability programs, access to the DAWNZERA Direct digital companion and other ongoing services and resources to help patients stay on track. Visit DAWNZERA.com for more information.

Webcast
Ionis will hold a webcast today at 12:15pm ET to discuss the FDA approval. Interested parties may access the webcast here. A webcast replay will be available for a limited time.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
DAWNZERA is contraindicated in patients with a history of serious hypersensitivity reactions, including anaphylaxis, to donidalorsen or any of the excipients in DAWNZERA.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions
Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with DAWNZERA. If signs and symptoms of serious hypersensitivity reactions occur, discontinue DAWNZERA and institute appropriate therapy.

ADVERSE REACTIONS
Most common adverse reactions (incidence ≥ 5%) are injection site reactions, upper respiratory tract infection, urinary tract infection, and abdominal discomfort.

Please see full Prescribing Information for DAWNZERA.

About DAWNZERA™ (donidalorsen)
DAWNZERA™ (donidalorsen) is approved by the U.S. Food and Drug Administration for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older. DAWNZERA is an RNA-targeted medicine designed to target plasma prekallikrein (PKK), which plays an important role in activating inflammatory mediators associated with acute attacks of HAE. For more information about DAWNZERA, visit DAWNZERA.com.

About Ionis Pharmaceuticals, Inc.
For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis has marketed medicines and a leading pipeline in neurology, cardiology and other areas of high patient need. As the pioneer in RNA-targeted medicines, Ionis continues to drive innovation in RNA therapies in addition to advancing new approaches in gene editing. A deep understanding of disease biology and industry-leading technology propels our work, coupled with a passion and urgency to deliver life-changing advances for patients. To learn more about Ionis, visit Ionis.com and follow us on X (Twitter), LinkedIn and Instagram.

Ionis Forward-Looking Statements
This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of DAWNZERA, our commercial medicines, additional medicines in development

and technologies. 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 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. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. 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, 2024, and most recent Form 10-Q, 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.

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