Ionis poised for continued momentum in 2024 with product launches and key advances in robust pipeline of investigational medicines for serious diseases

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– Numerous value-driving commercial, regulatory and pipeline milestones anticipated –

CARLSBAD, Calif., Jan. 8, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced highlights from the Company's 2023 achievements and previewed a number of important milestones expected in 2024. Ionis will provide a business update at the 42nd Annual J.P. Morgan Healthcare Conference on Wednesday, January 10 at 3pm PT; the presentation is available today on the Ionis website.

In 2023, Ionis made significant progress in advancing a steady cadence of medicines for people with serious diseases, including the U.S. approval of WAINUA™ (eplontersen) for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTRv-PN) and the accelerated approval of QALSODY® (tofersen) for SOD-1 amyotrophic lateral sclerosis (ALS). Ionis also shared positive Phase 3 trial readouts for WAINUA and for investigational olezarsen in familial chylomicronemia syndrome (FCS), a rare, life-threatening disease characterized by severely elevated triglycerides; olezarsen is also being evaluated in an ongoing Phase 3 program in severe hypertriglyceridemia. The late-stage pipeline expanded to nine medicines in Phase 3 trials for 11 potential indications and Ionis reported a number of additional positive data readouts. Ionis also continued to make key advances in its industry-leading technology platform, which now includes multiple RNA modalities and gene editing to support the next wave of medicines.

"With the recent approval of our first co-commercialized medicine, WAINUA for ATTRv-PN, and the potential for our first independent commercial launch with olezarsen in FCS later this year, Ionis is delivering on our vision to unlock better futures for people with serious diseases by building a leading fully-integrated, science-driven biopharmaceutical company," said Brett P. Monia, Ph.D., Ionis' chief executive officer. "We expect 2024 to be another robust year of execution and achievement, beginning with topline Phase 3 results expected in the first quarter for donidalorsen in hereditary angioedema. Ionis also looks forward to many additional regulatory milestones, important readouts across our mid- and late-stage pipeline and continued technology advances in our leading RNA therapeutics platform."

2024 Anticipated Highlights Include:

- **Continued progress with WAINUA, Ionis' first co-commercialized medicine in collaboration with AstraZeneca in the U.S.:**
  - U.S. launch for ATTRv-PN in January
  - European Medicines Agency (EMA) approval decision; additional country approvals
  - Additional regulatory filings for ATTRv-PN
  - Continuing the fully enrolled, landmark CARDIO-TTRansform trial in ATTR-cardiomyopathy, with data expected as early as 2025
- **Advancing olezarsen, our first anticipated independent launch:**
  - Detailed Phase 3 FCS results presentation
  - U.S. Food and Drug Administration (FDA) regulatory filing in FCS, potential approval decision (assuming priority review) and U.S. launch
  - EMA filing for FCS
  - Completion of enrollment in severe hypertriglyceridemia Phase 3 studies, with data expected in 2025
- **Pivotal results and potential regulatory filing for investigational donidalorsen, our second anticipated independent launch:**
  - Phase 3 OASIS-HAE in first quarter and OASIS-Plus switch results by mid-year
  - Potential U.S. regulatory filing in hereditary angioedema
- **Advancing additional independent investigational medicines:**
  - Ionis expects to have six independent neurology programs in clinical development by year-end 2024, including new programs in rare pediatric diseases and severe dementias, which currently have no approved therapies
  - Phase 2 results for ION224 in nonalcoholic steatohepatitis anticipated
- **Continued progress with key partnered programs, including:**
  - QALSODY: EU SOD1-ALS CHMP and approval decision (Biogen)
  - ION582: Phase 1/2 clinical results in Angelman syndrome (Biogen)
  - ION541: Phase 2 results in ALS (Biogen)

- IONIS-FB-L_{Rx}: Phase 2 results in IGA nephropathy and geographic atrophy, a serious eye disease (Roche)

For more information about QALSODY, visit https://www.qalsody.com/. This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with QALSODY. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

INDICATION for WAINUA™ (eplontersen)

WAINUA injection, for subcutaneous use, 45 mg is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

IMPORTANT SAFETY INFORMATION for WAINUA™(eplontersen)

WARNINGS AND PRECAUTIONS
Reduced Serum Vitamin A Levels and Recommended Supplementation WAINUA leads to a decrease in serum vitamin A levels. Supplement with recommended daily allowance of vitamin A. Refer patient to an ophthalmologist if ocular symptoms suggestive of vitamin A deficiency occur.

ADVERSE REACTIONS
Most common adverse reactions (≥9% in WAINUA-treated patients) were vitamin A decreased (15%) and vomiting (9%).

Please see link to U.S. Full Prescribing Information for WAINUA.

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 Ionis' 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 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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