Ionis showcases transformational medicines and industry-leading pipeline at Innovation Day

October 7, 2025

– Two independent launches underway in less than nine months, with two more on track for 2026 –

– Growing pipeline of wholly owned medicines in neurology and cardiometabolic disease and leading technology for next-generation medicines –

– Clear path to sustained positive cash flow –

– Ionis to webcast Innovation Day at 8:30 a.m. ET –

CARLSBAD, Calif.--(BUSINESS WIRE)--Oct. 7, 2025-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today is hosting its 2025 Innovation Day in New York City. Ionis leaders will highlight the company's recent and near-term independent launches, growing pipeline of wholly owned medicines, innovative technology and clear path to sustained positive cash flow. Additionally, a leading physician will discuss the current treatment landscape and substantial unmet needs for severe hypertriglyceridemia (sHTG) in advance of the potential olezarsen launch.

"In less than nine months, we achieved two independent launches, marking significant progress toward our goal of transforming human health by bringing RNA-targeted medicines to people with serious diseases," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "Our accelerating growth is driven by an industry-leading pipeline, with two more independent launches planned for 2026, four partner launches by the end of 2027 and continued advancement of our leading technology platform to deliver next-generation medicines. Innovation Day highlights how Ionis is creating substantial and enduring value for patients and shareholders through groundbreaking science and the ability to deliver medicines now and in the future."

Event location, webcast and replay information

The event will take place from 8:30 a.m. to 12:30 p.m. Eastern Time and will be webcast. Please click here to register for the event. A webcast replay will be available for a limited time at the Investor Events section of Ionis' website.

Ionis owned program highlights:

Building a leading cardiometabolic disease portfolio

- Ionis' **TRYNGOLZA® (olezarsen) launch in familial chylomicronemia syndrome (FCS)** in the U.S. is off to a strong start, with robust patient uptake, favorable physician engagement and positive access dynamics. Additionally, TRYNGOLZA was recently approved in the EU, with Sobi leading the commercial launch.
- Positive topline data from the Phase 3 CORE and CORE2 studies showed that **olezarsen for severe hypertriglyceridemia (sHTG)** achieved a highly statistically significant placebo-adjusted reduction of up to 72% in fasting triglycerides and an 85% reduction in acute pancreatitis events with favorable safety and tolerability. **Full data** will be presented during a late-breaking session **at the American Heart Association Scientific Sessions on November 8**. Based on these data, Ionis is planning to submit a supplemental new drug application to the U.S. Food and Drug Administration (FDA) by the end of the year.
- Robert D. Fishberg, M.D., cardiologist with Atlantic Medical Group in Springfield, NJ and assistant clinical professor of medicine at the Sidney Kimmel Medical College, Thomas Jefferson University, will discuss the current treatment landscape and substantial unmet needs for sHTG in advance of the potential olezarsen sHTG launch in 2026.
- Extending its leadership in **triglyceride management**, Ionis will share positive interim Phase 1 results of **ION775, an apoC-III siRNA** with the potential for semiannual dosing and Ionis' first clinical-stage siRNA medicine. ION775 achieved substantial, durable and sustained reductions in apoC-III and fasting triglycerides with favorable safety and tolerability in healthy volunteers with moderately elevated triglycerides. Ionis is on track to initiate a Phase 2 study in 2026.

DAWNZERA: Transforming the HAE treatment paradigm

- The U.S. launch of Ionis' **DAWNZERA™ (donidalorsen), the first and only RNA-targeted treatment for hereditary angioedema (HAE),** is off to an encouraging start and marks the second independent launch for Ionis. Patient starts are occurring across the U.S. from patients switching from established long-term prophylactic treatments, patients previously only on acute treatment and those who are naïve, with strong initial payer engagement. The EU launch, to be led by

Otsuka, is anticipated in 2026.
- Multiple Ionis presentations will be shared at the American College of Allergy, Asthma, & Immunology Annual Scientific Meeting on November 6-10, including one-year results from the Phase 3 OASISplus open-label extension study and one-year switch cohort results from OASISplus.

Advancing our leading neurology portfolio

- Ionis is well-positioned to deliver a steady cadence of neurology medicines with a strong pipeline of wholly owned medicines. Ionis' first independent launch for a neurological disease (zilganersen) is expected in 2026.
- Ionis will share additional details today about the positive topline results from the pivotal study of **zilganersen for Alexander disease**, a rare, progressive and often fatal neurological condition with no approved disease-modifying treatments. Ionis plans to submit a new drug application to the FDA in Q1 2026 and present additional data at an upcoming medical conference.
- Ionis will also share new, positive 18-month long-term extension data from the Phase 2 HALOS study of **ION582 for Angelman syndrome**, a severe neurodevelopmental disorder with no approved disease-modifying treatments.
- The Phase 3 REVEAL study of **ION582 for Angelman syndrome** is expected to be fully enrolled in 2026. ION582 recently received U.S. Breakthrough Therapy designation.
- Ionis will share its next expected clinical-stage wholly owned neurology medicine, **ION337 for Dravet syndrome**, a serious, rare, genetic form of epilepsy with no approved disease-modifying treatments. ION337 utilizes Ionis proprietary technology that enhances the potency and durability of antisense oligonucleotides (ASOs) that modulate splicing.

Creating substantial value through accelerating growth

- Ionis has a **strong financial foundation** with ~$2B in cash and short-term investments (2025 financial guidance), efficient capital structure and a strong history of disciplined capital management.
- Ionis' accelerating revenue growth opportunity is fueled by its recent launches and late-stage medicines that provide > $5B in potential annual peak revenue (comprised of >$3B in annual peak independent product revenue and >$2B in annual peak royalties from partnered medicines).
- With accelerating growth within reach, Ionis has a clear path to achieve sustained positive cash flow and is expected to reach cash flow breakeven in 2028.

Partnered program highlights:

- In 2026, there are four key Phase 3 readouts planned in areas of high unmet need:
  - Data from the B-Well 1 and B-Well 2 studies of **bepirovirsen** for **hepatitis B virus (HBV)** are expected in H1 (GSK).
  - Data from the Lp(a) HORIZON study of **pelacarsen** for **lipoprotein(a) (Lp(a))-driven cardiovascular disease (CVD)** are expected in H1 (Novartis).
  - Data from the CARDIO-TTRansform study of **eplontersen** for **transthyretin-mediated amyloid cardiomyopathy (ATTR-CM)** are expected in H2 (AstraZeneca).
  - Data from the IMAGINATION study of **sefaxersen** for **IgA nephropathy (IgAN)** are expected in 2026 (Roche).

Ionis' Marketed Medicines

INDICATION for TRYNGOLZA® (olezarsen)

TRYNGOLZA® (olezarsen) was approved by the U.S. Food and Drug Administration as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

TRYNGOLZA is contraindicated in patients with a history of serious hypersensitivity to TRYNGOLZA or any of the excipients in TRYNGOLZA. Hypersensitivity reactions requiring medical treatment have occurred.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions (including symptoms of bronchospasm, diffuse erythema, facial swelling, urticaria, chills and myalgias) have been reported in patients treated with TRYNGOLZA. Advise patients on the signs and symptoms of hypersensitivity reactions and instruct patients to promptly seek medical attention and discontinue use of TRYNGOLZA if hypersensitivity reactions occur.

ADVERSE REACTIONS

The most common adverse reactions (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count and arthralgia.

Please see full Prescribing Information for TRYNGOLZA.

INDICATION for DAWNZERA™ (donidalorsen)

DAWNZERA (donidalorsen) is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older.

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 Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has marketed medicines and a leading pipeline in neurology, cardiometabolic disease and select 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 our business, financial guidance and the therapeutic and commercial potential of our commercial medicines, additional medicines in development and technologies and our expectations regarding development and regulatory milestones. 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. 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 our Form 10-K for the year ended December 31, 2024, and our most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of these and other documents are available at www.ionis.com.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals and its subsidiaries.

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