Ionis shares significant business and pipeline progress at Innovation Day, highlighting strength of capabilities from research and technology through commercialization

October 4, 2023

- *With experienced commercial team in place, Ionis poised to independently bring steady cadence of potentially transformational RNA-targeted medicines to patients beginning in 2024*
- *Plan to add four new wholly owned neurology medicines to clinical pipeline by end of 2024*
- *Innovative technology advances unlocking new opportunities in neurology and cardiology as well as in new therapeutic areas*
- *With multiple launches anticipated over the coming years, Ionis positioned for next-level value creation driven by significant revenue growth and positive cash flow*
- *Ionis to webcast Innovation Day today at 8:00 a.m. ET*

CARLSBAD, Calif., Oct. 4, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) is holding an investor and analyst event, Ionis Innovation Day: Discovering, Developing and Delivering Transformational Medicines, in New York City today. Presentations from Ionis leaders and external physicians will highlight Ionis' comprehensive integrated research, development, and commercialization capabilities, along with key pipeline and technology highlights.

"Our leadership in RNA-targeted medicine includes multiple modalities empowering us to advance the right medicines for the right targets," said Brett P. Monia, Ph.D., Ionis' chief executive officer. "Our powerful and prolific research and development engine has discovered groundbreaking medicines for people with devastating diseases. We have matched this engine with a talented commercial organization poised to deliver a steady flow of wholly owned medicines to patients. With last week's announcement of positive Phase 3 data for olezarsen in people with familial chylomicronemia syndrome (FCS), we're moving ahead with preparations for the first of multiple anticipated independent commercial launches."

Event location, webcast and replay information

The event will take place at the Westin New York Grand Central from 8:00 a.m. to 3:00 p.m. Eastern Time and will also be webcast. Please click here to register for the event. A webcast replay will be available within 48 hours after the event at https://ir.ionispharma.com/events-and-presentations/upcoming-events.

Highlights include:

Near-Term Commercial Medicines

- Ionis has made important progress in building our commercial and medical affairs organizations led by individuals with deep, relevant expertise across rare and broad diseases.
- With the **eplontersen** PDUFA date of Dec. 22, 2023 nearing for ATTR polyneuropathy (PN), Ionis is ready to bring this important new medicine to patients along with our partner AstraZeneca, if approved.
    - Eplontersen has the potential to be the treatment of choice, backed by strong efficacy and safety data, a self-administration profile and a strong global alliance with AstraZeneca.
    - Last week, positive Phase 3 NEURO-TTRansform data were published in *The Journal of the American Medical Association,* and regulatory filings are planned in the EU and other countries this year and next.
    - The Phase 3 CARDIO-TTRansform trial, the largest trial ever conducted in ATTR cardiomyopathy patients, is fully enrolled and expected to read out as early as 1H 2025.
- **Olezarsen** is poised to be Ionis' **first wholly owned independent commercial launch.**
    - Last week, Ionis announced positive Phase 3 olezarsen Balance results in FCS, showing statistically significant triglyceride lowering and a substantial reduction in acute pancreatitis events in addition to a favorable safety and tolerability profile. Based on these data, Ionis is planning to file U.S. and EU regulatory applications in early 2024.
    - Phase 3 studies continue for severe hypertriglyceridemia (SHTG), a more prevalent disease affecting more than three million people in the U.S.
    - Henry Ginsburg, M.D., Professor of Medicine, Columbia University, will speak at the event to share his perspectives on the acute need for new treatments to treat people with FCS and SHTG.
- **Donidalorsen** was recently granted U.S. Orphan Drug Designation.
    - Ionis plans to report Phase 3 results with donidalorsen for prophylactic treatment of hereditary angioedema (HAE) in the first half of 2024. Ionis also plans to report topline data from a second Phase 3 study evaluating switching from currently approved HAE treatments in mid-2024.
    - Two-year results from the Phase 2 open-label-extension trial showed that donidalorsen treatment resulted in a 96% overall sustained mean reduction from baseline in HAE attack rates. These data will be presented at a medical congress later this year.
    - Raffi Tachdjian, M.D., MPH, FAAAAI, FACAAI, Associate Clinical Professor of Medicine and Pediatrics UCLA School of Medicine; Chief, Division of Allergy and Immunology Providence St. John Medical Center will discuss the need for new prophylactic HAE treatments as more than one-third of patients on prophylactic treatment report more

than two attacks per month.

Next Wave of Wholly Owned Medicines

- Building on Ionis' proven track record in neurology with two approved medicines, 12 in clinical trials and more than 10 in lead optimization/preclinical development, Ionis is advancing a wholly owned neurology pipeline.
- The lead independent program, **zilganersen** for the treatment of Alexander disease, a serious genetic leukodystrophy, is now in Phase 3 development.
- In addition, Ionis will announce today that four new wholly owned medicines in rare pediatric neurological diseases and dementias are planned to enter first-in-patient studies by the end of 2024:
    - **ION356 (PLP1), for the treatment of children with Pelizaeus-Merzbacher Disease,** a severe leukodystrophy, which recently received Rare Pediatric Disease Designation and Orphan Drug Designation from the U.S. FDA;
    - **ION440 for the treatment of children with MeCP2 duplication syndrome**, which causes significant developmental delays, impaired motor function and seizures;
    - **ION717, for the treatment of prion disease**, which causes fatal dementia, is planned to enter a first-in-patient study in 2023;
    - And, an undisclosed **genetic dementia program,** which is currently in preclinical development.

Advancing Technologies to Reach More Patients in Need

- Ionis' leading medicinal chemistry platform is enabling technological advances to enhance existing medicine profiles and expand into new tissues and/or therapeutic areas.
    - Ionis is applying new chemistries such as the **Mesyl Phosphoramidate (MsPA) backbone** to improve the duration of effect and therapeutic index of investigational medicines.
    - The company is using **multiple drug modalities**, including **antisense (ASO) and small interfering RNA (siRNA)**, to identify the best potential medicine for a particular target and/or tissue.
    - **By leveraging targeted delivery approaches**, including Bicycle® technology via our collaboration with Bicycle Therapeutics, Ionis is developing medicines that have antibody-like selectivity with a low total molecular weight, which allows delivery to skeletal and cardiac muscle. Progress is also being made in delivering medicines across the blood-brain barrier with systemic dosing.

Clear Path to Unlocking Next-Level Value

- Ionis has a **solid financial foundation** with a strong balance sheet with ~$2B in cash, and existing substantial and sustained revenue streams.
- Ionis is **investing efficiently** to bring our near-term medicines to patients.
- Ionis anticipates that **revenue growth from multiple medicines as** well as **ongoing partner and royalty revenue** will drive future **positive cash flow**.

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 our business, financial guidance and the therapeutic and commercial potential of QALSODY™ (tofersen), SPINRAZA® (nusinersen), TEGSEDI® (inotersen), WAYLIVRA® (volanesorsen), eplontersen, olezarsen, donidalorsen, ulefnersen, zilganersen, pelacarsen, bepirovirsen, IONIS-FB-LRx, Ionis' technologies, and Ionis' 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 December 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.

View original content to download multimedia:https://www.prnewswire.com/news-releases/ionis-shares-significant-business-and-pipeline-progress-at-innovation-day-highlighting-strength-of-capabilities-from-research-and-technology-through-commercialization-301946469.html

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