Ionis announces positive interim data from partner Roche's Phase 3 IMAgINATION study in IgA nephropathy (IgAN)

September 23, 2026

– Sefaxersen demonstrated statistically significant and clinically meaningful reductions in proteinuria versus placebo at 37 weeks, showing best-in-class potential –

– IgAN is a progressive kidney disease that is typically diagnosed in young adults and up to 50% of people progress to kidney failure within 20 years, requiring dialysis or transplantation –

– Interim data will be presented at an upcoming medical meeting and shared with health authorities –

CARLSBAD, Calif.--(BUSINESS WIRE)--Sep. 23, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) and partner Roche today announced positive prespecified interim results from the ongoing Phase 3 IMAgINATION study evaluating investigational sefaxersen in adults with primary IgA nephropathy (IgAN). The study met its primary endpoint with sefaxersen achieving statistically significant and clinically meaningful improvements in proteinuria reduction, compared to placebo at 37 weeks, as measured by 24-hour urine protein-to-creatinine ratio (UPCR). Proteinuria is a key indicator of kidney damage, and a reduction in UPCR is strongly associated with the preservation of long-term kidney function. Sefaxersen is a once-monthly subcutaneous injection designed to enable self-administration for people with IgAN. The safety and tolerability profile of sefaxersen was consistent with previously reported data, with no new safety signals identified.

"With these positive interim results, sefaxersen is positioned to directly address a primary driver of IgAN-related kidney damage, offering the potential to help slow disease progression and potentially reduce the long-term need for dialysis or kidney transplantation," said Brett P. Monia, Ph.D., chief executive officer, Ionis. "These findings are an important advance for the field and further demonstrate the broad potential of our RNA-targeted technology to make a meaningful difference for people living with serious diseases."

The IMAgINATION study will continue as a blinded study to evaluate the change in kidney function over two years, as measured by estimated glomerular filtration rate (eGFR) at week 105. Interim analysis data will be presented at an upcoming medical congress and shared with health authorities, with the goal of bringing this treatment to patients as soon as possible.

IgAN, also known as Berger's disease, is a chronic and progressive autoimmune disease that leads to end-stage kidney disease in up to 50% of patients within 20 years after diagnosis. Typically diagnosed before the age of 40 years, it affects at least 25 adults per million worldwide each year.

Roche licensed sefaxersen from Ionis for the treatment of complement-mediated diseases. Under the terms of the agreement, Ionis received an upfront payment, license fee and development milestone payments and is eligible to receive regulatory and sales milestone payments as well as tiered royalties on net sales of sefaxersen.

About sefaxersen

Sefaxersen, an investigational, highly specific liver-directed antisense oligonucleotide that inhibits factor B production, is the first RNA-targeted therapy for IgA nephropathy (IgAN). Serum complement factor B levels are elevated in people with IgAN. Sefaxersen is designed to provide sustained control of the alternative complement pathway, an important pathway in IgAN, enabling once-monthly subcutaneous dosing and is intended for self-administration in people with IgAN.

About the IMAgINATION Study

IMAgINATION (NCT05797610) is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of subcutaneous sefaxersen, an investigational antisense inhibitor of complement factor B, in patients with primary IgA nephropathy at high risk of progression. The study enrolled 459 people, who are randomized 1:1 to receive sefaxersen or placebo for 105 weeks. Participants may switch to open-label treatment after week 105 at the investigator's discretion or after the common-close timepoint, whichever occurs first. The primary endpoint of the study is the change from baseline in the urine protein-to-creatinine ratio at 37 weeks.

About IgA Nephropathy (IgAN)

IgAN, also known as Berger's disease, is a serious, chronic and progressive autoimmune kidney disease affecting at least 25

adults per million worldwide each year and is typically diagnosed before the age of 40 years. In IgAN, immune complexes deposit in the kidneys, which activates the complement system's alternative pathway, leading to inflammation and subsequent kidney damage. It is the most common form of primary glomerulonephritis (inflammation of kidney glomeruli) and remains a leading cause of kidney failure, with up to 50% of patients experiencing end-stage kidney disease within 20 years of diagnosis. Many current therapies aim to reduce protein levels in the urine and control blood pressure to slow progression of the disease.

Updated KDIGO 2025 guidelines* highlight the need to address both the underlying immune-mediated causes of IgAN and the downstream consequences of kidney damage. While new therapies have expanded treatment options, important unmet needs remain, including improved long-term preservation of kidney function and more targeted approaches that address key drivers of disease progression.

About Ionis Pharmaceuticals, Inc.

For more than 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 Ionis' business and the therapeutic and commercial potential of sefaxersen, 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 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, 2025 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.

*KDIGO guidelines serve as the foundational framework for healthcare organizations, policymakers and clinicians worldwide to standardize kidney disease diagnosis, staging and treatment.

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