



Ionis announces European licensing agreement with Otsuka for donidalorsen in hereditary angioedema

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- *Otsuka to leverage strong commercial infrastructure and rare disease experience to reach European HAE patients*
- *Ionis plans to independently bring donidalorsen to U.S. patients if approved*
- *Donidalorsen Phase 3 results expected in the first half of 2024*

CARLSBAD, Calif., Dec. 18, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that it has entered into a license agreement with Otsuka Pharmaceutical Co., Ltd. (Otsuka) under which Otsuka obtains exclusive rights in Europe to commercialize donidalorsen, an investigational prophylactic treatment for hereditary angioedema (HAE). Ionis will maintain responsibility for the non-clinical and clinical development of donidalorsen, and Otsuka will be responsible for European regulatory filings and commercialization.



Ionis plans to independently launch donidalorsen in the U.S. if approved, as part of the company's strategy to deliver a steady flow of wholly owned medicines to patients.

"We are excited to collaborate with Otsuka given their proven results in bringing rare disease medicines to patients in Europe," said Brett P. Monia, Ph.D., Ionis' chief executive officer. "This agreement is aligned with our strategy to initially focus our commercialization efforts on the U.S. market. We are encouraged by the strong product profile of donidalorsen to date and look forward to reporting pivotal topline Phase 3 donidalorsen results in HAE in the first half of next year."

Otsuka brings expertise in delivering rare disease medicines to patients, a robust commercial infrastructure, and deep knowledge of regional and local regulations across European countries. As part of the agreement, Ionis will receive a \$65 million upfront payment and milestone payments based on achievement of regulatory and sales targets. Ionis is also eligible to earn tiered royalties ranging from 20 to 30 percent (based on aggregate annual net sales).

Makoto Inoue, president and representative director of Otsuka Pharmaceutical Co., Ltd. commented, "Otsuka has developed drugs in Europe for rare diseases such as autosomal dominant polycystic kidney disease (ADPKD). Through this collaboration with Ionis, a leader in RNA-targeted therapy, if regulatory approval is received, we look forward to bringing donidalorsen to patients in Europe to address the unmet medical needs of patients with HAE."

Ionis recently reported two-year results from the Phase 2 open-label extension (OLE) trial showing that donidalorsen treatment resulted in a 96% overall sustained mean reduction from baseline in HAE attack rates and was recently granted Orphan Drug Designation in the U.S.

Injection site (IS) discoloration and IS reaction were the only study drug-related treatment-emergent adverse events (TEAEs) reported in more than one patient (n=2, 11.8% each). No serious adverse events were reported in the OLE study, and no TEAEs led to study discontinuation. The company plans to report Phase 3 results with donidalorsen for prophylactic treatment of HAE in the first half of 2024.

About Hereditary Angioedema (HAE)

HAE is a rare and life-threatening genetic disease characterized by unpredictable and frequently severe swelling of the skin, gastrointestinal (GI) tract, upper respiratory system, face, and throat, which can be life-threatening.¹⁻⁵ HAE is estimated to affect more than 20,000 patients in the U.S. and Europe.⁶ In the U.S., doctors frequently use prophylactic treatment approaches to prevent and reduce the severity of HAE attacks in patients.

About Donidalorsen

Donidalorsen is an investigational **L**igand-**C**onjugated **A**ntisense (LICA) medicine designed to target the prekallikrein, or PKK, pathway. PKK plays an important role in activating inflammatory mediators associated with acute attacks of hereditary angioedema (HAE). By reducing the production of PKK, donidalorsen could be an effective prophylactic approach to preventing HAE attacks.

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 Ionis' business, and the therapeutic and commercial potential of donidalorsen, Ionis' technologies, and 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 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.

Ionis Pharmaceuticals® is a registered trademark of Ionis Pharmaceuticals, Inc.

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