



Ionis announces European Medicines Agency accepts Marketing Authorization Application of tofersen to treat rare, genetic form of ALS

December 5, 2022

- *SOD1-ALS affects approximately 2% of people living with ALS worldwide¹*
- *If approved, tofersen would be the world's first treatment to target a genetic cause of ALS*
- *EMA acceptance follows FDA's acceptance of tofersen NDA earlier this year*

CARLSBAD, Calif., Dec. 5, 2022 /PRNewswire/ -- [Ionis Pharmaceuticals, Inc.](#) (Nasdaq: IONS) today announced that the European Medicines Agency (EMA) has accepted the marketing authorization application (MAA) for review of tofersen, an investigational medicine for the treatment of superoxide dismutase 1 (SOD1) amyotrophic lateral sclerosis (ALS). SOD1-ALS is a progressive and uniformly fatal disease that affects fewer than 1,000 people across Europe.²



The EMA is the second regulatory agency to accept review of a marketing application for tofersen following U.S. Food and Drug Administration (FDA) acceptance earlier this year. The FDA has set a PDUFA date for tofersen of April 25, 2023. There are currently no treatments targeted for SOD1-ALS.

"EMA acceptance of the tofersen MAA is a significant development for people and families battling SOD1-ALS," said C. Frank Bennett, Ph.D., executive vice president, chief scientific officer and franchise leader for neurological programs at Ionis. "If approved, tofersen will be the world's first treatment that targets a genetic cause of ALS. Tofersen also strengthens Ionis' platform strategy to target other neurological diseases, including other forms of ALS."

The MAA includes results from the Phase 3 VALOR study, its open label extension (OLE) study, a Phase 1 study in healthy volunteers and a Phase 1/2 study evaluating ascending dose levels. Also included are the most current 12-month integrated results from VALOR and the OLE study that were recently published in [The New England Journal of Medicine](#).

Biogen announced that it will maintain its early access program for tofersen, which is now available in 34 countries. Biogen also announced that it will continue to actively engage with other regulators around the world and will provide updates when appropriate.

About Tofersen

Tofersen is an antisense medicine being evaluated for the potential treatment of SOD1-ALS. Tofersen binds to SOD1 mRNA, allowing for its degradation by RNase-H in an effort to reduce synthesis of SOD1 protein production. In addition to the ongoing open label extension of VALOR, tofersen is being studied in the Phase 3 ATLAS study designed to evaluate whether tofersen can delay clinical onset when initiated in presymptomatic individuals with a SOD1 genetic mutation and biomarker evidence of disease activity. Biogen licensed tofersen from Ionis under a collaborative development and license agreement.

About Amyotrophic Lateral Sclerosis and SOD1-ALS

Amyotrophic lateral sclerosis (ALS) is a rare, progressive and fatal neurodegenerative disease that results in the loss of motor neurons in the brain and the spinal cord that are responsible for controlling voluntary muscle movement. People with ALS experience muscle weakness and atrophy, causing them to lose independence as they steadily lose the ability to move, speak, eat, and eventually breathe. Average life expectancy for people with ALS is three to five years from time of symptom onset. Patients with some SOD1 mutations have an even shorter life expectancy.

Multiple genes have been implicated in ALS. Genetic testing helps determine if a person's ALS is associated with a genetic

mutation, even in individuals without a family history of the disease. Currently, there are no genetically targeted treatment options for ALS. Mutations in the SOD1 gene are responsible for approximately 2% of the estimated 168,000 people who have ALS globally (SOD1-ALS).

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry-leading cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming a leading, fully integrated biotechnology company.

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 Ionis' technologies, tofersen 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 those related to the impact COVID-19 could have on our business, and 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, 2021, and the most recent Form 10-Q quarterly filing, 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" refers to Ionis Pharmaceuticals and its subsidiaries.

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

¹ Brown CA, Lally C, Kupelian V, Flanders WD. Estimated Prevalence and Incidence of Amyotrophic Lateral Sclerosis and SOD1 and C9orf72 Genetic Variants. *Neuroepidemiology*. 2021;55(5):342-353. doi: 10.1159/000516752. Epub 2021 Jul 9.

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