

Ionis enters exclusive licensing agreement with Bicycle Therapeutics aimed at further advancing LICA technology

July 13, 2021

- Exclusive rights to innovative peptide technology positions Ionis to further strengthen targeting capabilities of its LICA therapies

CARLSBAD, Calif., July 13, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today announced that it has entered into an exclusive licensing agreement with Bicycle Therapeutics plc (NASDAQ: BCYC) to increase the delivery capabilities of Ionis' advanced **L**igand **C**onjugated **A**ntisense (LICA) medicines. The agreement provides Ionis exclusive access to Bicycle's proprietary macrocyclic peptides, referred to as *Bicycles*, to design LICAs that target transferrin receptor 1 for use with oligonucleotides. This LICA strategy has demonstrated both the improved delivery of antisense medicines to muscle tissue, including cardiac muscle, as well as the potential to cross the blood brain barrier.

Bicycle Therapeutics is a clinical-stage biopharmaceutical company developing a novel class of medicines, *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are fully synthetic short peptides constrained with small molecule scaffolds to form two loops that stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making *Bicycles* attractive candidates for drug development.

"One of our key strategic objectives is to expand our drug discovery capabilities. The agreement with Bicycle Therapeutics represents a strategic addition to our expanding LICA platform, giving us the potential to meaningfully expand our drug discovery capabilities and deliver many more transformational medicines to the market," said Brett P. Monia, Ph.D., Ionis' chief executive officer. "We believe that investing in technologies like Bicycle's cutting-edge transferrin receptor 1-targeting peptides will enhance our ability to design medicines to tackle devastating diseases in need of better treatment options."

"Our collaboration with Bicycle will accelerate Ionis' progress toward creating best-in-class, low molecular weight ligands for muscle-specific targeted delivery," said Eric E. Swayze, Ph.D., executive vice president of research at Ionis. "This approach offers several potential advantages over related strategies in development, including increased potency, more convenient administration, less complex manufacturing processes and reduced cost of goods." Dr. Swayze added, "We are pleased with the data we have generated to date and look forward to incorporating optimized Bicycle peptides into our LICA delivery platform."

Under terms of the agreement, Ionis obtained an exclusive license to Bicycle's technology covering the entire class of transferrin receptor 1 *Bicycles* for use in targeted delivery of oligonucleotide drugs. Ionis made a \$45 million upfront payment to Bicycle which included a license fee, an option fee, and an \$11 million equity investment in Bicycle. Bicycle will be eligible to earn development and regulatory milestone payments on a program-by-program basis and royalties on product sales.

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 neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

To learn more about Ionis visit www.ionispharma.com and follow us on Twitter @ionispharma.

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of Ionis' technologies and 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 December 31, 2020, and the most recent Form 10-Q quarterly filing, which are on file with the SEC. 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.

 View original content to download multimedia: <https://www.prnewswire.com/news-releases/ionis-enters-exclusive-licensing-agreement-with-bicycle-therapeutics-aimed-at-further-advancing-lica-technology-301332026.html>

SOURCE Ionis Pharmaceuticals, Inc.

Ionis Pharmaceuticals Media Contact: Roslyn Patterson, Vice President, Marketing and Communications, 760-603-4679; Ionis Investor Relations Contact: 760-603-2331