Ionis Enters into Collaboration with Ribo to Advance RNA-Targeted Therapeutics in China

- *Ionis gains a key partner in China to develop up to three Generation 2+ antisense drugs in metabolic disease and cancer*
- *Ribo to commit significant resources to advance Ionis' single-stranded RNAi (ssRNAi) technology*
- *Ionis retains rights to develop and commercialize ssRNAi technology and all drugs under the collaboration outside of China*

CARLSBAD, Calif., April 18, 2017–Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today announced a collaboration and license agreement with Suzhou Ribo Life Science Co., Ltd. (Ribo) to develop and commercialize RNA-targeted therapeutics in China. Ionis granted Ribo a license for the right to commercialize in China two Ionis Generation 2+ antisense drugs in metabolic disease and cancer and an option to license a third pre-specified Generation 2+ antisense drug. In addition, Ribo will be responsible for conducting a multi-year research and drug discovery program to identify drugs that utilize Ionis' ssRNAi technology. Ionis will receive an undisclosed up-front payment and equity in Ribo. Ionis retains the rights to develop and commercialize ssRNAi technology and all drugs under the collaboration outside of China.

"The need for new medicines in China is growing rapidly, especially for metabolic diseases and certain genetically-defined cancers," said Brett Monia, senior vice president of drug discovery and franchise leader for oncology and rare diseases at Ionis Pharmaceuticals. "Ribo is the ideal partner for us in China. Ribo has made excellent progress in its RNAi therapeutic programs and we believe we will benefit from their drug development and regulatory expertise in China. We believe that our partnership with Ribo maximizes the value of our drugs in this collaboration by leveraging the clinical data generated in China to support the overall global development plan for each drug."

"We are committed to advancing new RNA-targeted therapeutics, like RNAi and antisense, to patients with high unmet medical need in China," said Liang Zicai, founder and Chairman of Ribo. "Ionis has made significant breakthroughs showing that chemically modified single-stranded oligonucleotides can activate the RNAi pathway. We believe that this work is the foundation for a robust drug discovery platform that takes advantage of using single-stranded RNA-like antisense drugs that harness the power of the RNAi pathway. We are excited by the opportunity to contribute our expertise and resources to advancing this promising technology."

Following the identification of a development candidate, Ribo may exercise its option to license each drug by paying Ionis a license fee. For each drug that Ribo licenses, Ribo will be responsible for all development and commercialization activities and costs in China. Ionis is eligible to receive development, regulatory and commercial milestone payments as each drug advances. In addition, Ionis is eligible to receive royalties on net sales of each drug.

Ribo will provide Ionis a royalty-free license to the data and intellectual property created under the collaboration.

ABOUT RNAi AND ssRNAi

As it is known to occur in nature, the RNAi pathway is mediated by short double-stranded RNA oligonucleotides called "small interfering RNAs" or "siRNAs." To date, efforts aimed at harnessing this pathway to silence disease-causing proteins have used double-stranded siRNAs. Double-stranded siRNA drugs require complex formulations or special conjugates to achieve sufficient delivery for systemic activity. This requirement has severely limited the development of safe and effective drugs that work through the RNAi pathway. In contrast, single-stranded RNA-like antisense drugs can be administered subcutaneously and distribute to tissues without the need for complex formulations or special conjugates. Using its expertise in oligonucleotide chemistry and design, Ionis has discovered strategies for designing single-stranded oligonucleotides that act through the RNAi mechanism. With further development, these chemically modified, single-stranded, RNA-like oligonucleotides have the potential for improved properties for systemic administration while harnessing the advantages of the RNAi mechanism.

ABOUT SUZHOU RIBO LIFE SCIENCE CO., LTD.

Suzhou Ribo Life Science Co., Ltd. is an innovative R&D company devoted to the development of nucleic acid drugs and related products based on the RNA interference (RNAi) technology. With its innovative R&D capabilities, Ribo has built a strong R&D pipeline with numerous drug products in different stages, aiming to contribute to the treatment of serious diseases troubling the Chinese population. Ribo has also built a strong foundation in nucleic acid liquid-phase synthetic technology and manufacture of nucleic acid drug substances. Ribo's founders include some of China's most renowned scientists in the field of RNAi technology. Ribo received the prize of The First Innovative Team in Jiangsu China. Ribo is headquartered in Kunshan, Jiangsu Province and has a subsidiary in Beijing. For more information, please visit www.ribolia.com.

ABOUT IONIS PHARMACEUTICALS, INC.

Ionis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Ionis has created a large pipeline of first-in-class or best-in-class drugs, with over three dozen drugs in development. SPINRAZA™ (nusinersen) is a drug that has been approved in the U.S. for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. Biogen is responsible for commercialization of SPINRAZA. Drugs currently in Phase 3 development include volanesorsen, a drug Ionis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy; and IONIS-TTR$_{Rx}$, a drug Ionis is developing with GSK to treat patients with TTR amyloidosis. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

IONIS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Ionis' collaboration with Ribo, and the discovery, development, activity, therapeutic and commercial potential and safety of drugs under Ionis' relationship with Ribo. 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, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. 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, 2016, which is on file with the SEC. Copies of this 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.

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