

# Biogen and Ionis Expand Strategic Collaboration to Develop Drug Candidates for a Broad Range of Neurological Diseases

April 20, 2018

- Transaction builds upon the productive collaboration that produced SPINRAZA<sup>®</sup> as well as two antisense drug candidates currently in the clinic, with the potential to advance up to seven more drug candidates to the clinic within the next two years
- The antisense platform developed by Ionis is an established and validated gene-based therapeutic modality, as evidenced by the success of SPINRAZA, with the potential to address numerous neurological diseases that are currently untreatable
- Biogen will pay Ionis \$1 billion in cash, including an equity investment in Ionis stock and an upfront payment, representing one of the most significant discovery stage collaborations in the industry

CAMBRIDGE, Mass. & CARLSBAD, Calif.--(BUSINESS WIRE)--Apr. 20, 2018-- [Biogen](#) (Nasdaq: BIIB) and Ionis Pharmaceuticals (Nasdaq: IONS) announced today they have expanded their strategic collaboration through a new ten-year collaboration agreement to develop novel antisense drug candidates for a broad range of neurological diseases. This collaboration capitalizes on Biogen's expertise in neuroscience research and drug development and Ionis' leadership in RNA targeted therapies with the goal of developing a broad pipeline of investigational therapies. It builds upon a productive collaboration that produced SPINRAZA, the first and only approved treatment for patients with spinal muscular atrophy.

Today, April 20, 2018, Biogen and Ionis will host company conference calls and webcasts to discuss the new collaboration. Full webcast details can be found below.

Under the terms of the collaboration, Biogen will pay Ionis \$1 billion in cash, which will include \$625 million to purchase 11,501,153 shares of Ionis common stock at a price of \$54.34 per share, at an approximately 25% cash premium, and a \$375 million upfront payment. Biogen will have the option to license therapies arising out of this collaboration and will be responsible for their development and commercialization. In addition, Biogen may pay milestone payments, license fees and royalties on net sales.

The companies plan to advance programs for a broad range of neurological diseases for which few treatment options exist today. Disease areas include dementia, neuromuscular diseases, movement disorders, ophthalmology, diseases of the inner ear, and neuropsychiatry. Biogen will have the first choice of neurology targets on which to exclusively collaborate with Ionis. In this collaboration, Ionis will be responsible for the identification of antisense drug candidates based on selected targets, while Biogen will be responsible for and pay for non-clinical studies, clinical development, manufacturing, and commercialization.

"Biogen and Ionis share a commitment and passion to bring new therapeutic options to those living with neurological diseases where the unmet medical need is high and growing," said Michel Vounatsos, chief executive officer of Biogen. "We believe that this new collaboration will allow us to meaningfully expand our neuroscience pipeline in a way that differentiates Biogen. With the large number of diseases that could benefit from Ionis' antisense platform, we believe that the time is now to build upon our highly productive collaboration with Ionis as we aim to transform the treatment of neurological diseases around the world."

"There is no better partner for Ionis to develop new antisense drugs to treat neurological diseases than Biogen. Their demonstrated perseverance, dedication, and commitment to innovation in developing drugs for these challenging diseases is unmatched," said Stanley T. Croke, M.D., chief executive officer and chairman of Ionis. "These attributes and Biogen's investment in neurological diseases have been important to the successes we've achieved already in the collaboration. Working with Biogen, we have achieved what neither company could have achieved alone. Together, we believe we can create a robust neurological disease franchise fueled by Ionis' antisense technology and highlighted by the tremendous success of SPINRAZA. This new collaboration provides the potential opportunity to build an even stronger pipeline for Biogen and Ionis, with the expectation of bringing further benefit to patients in desperate need and value to Ionis' shareholders. This new collaboration's financial terms, upfront payment, milestone payments, and royalties are substantially higher compared to our previous collaborations with Biogen, which demonstrates the value we have created in applying Ionis' antisense technology platform to neurological disease. We believe Biogen's equity investment reflects its commitment to Ionis, to antisense technology, and to the success of this collaboration."

"The transformational success of SPINRAZA has given us increased confidence that antisense therapeutics have the potential to address many diseases of the central nervous system that were previously untreatable," said Michael Ehlers, M.D., Ph.D., executive vice president, Research and Development at Biogen. "Due to the ability of antisense oligonucleotides to directly intervene at the genetic origin of disease, we believe this approach could have a higher probability of success than traditional modalities, with a potentially more efficient development path to more rapidly help patients who suffer from diseases with limited or no treatment options. Our experience with antisense therapeutics makes us believe that they will be the preferred drug modality for numerous genetic diseases and targets of the nervous system."

"Our collaboration with Biogen has provided significant value for both companies. We have and continue to learn more about neurological diseases and successful strategies for developing drugs for these diseases. Biogen has worked with us to validate biomarkers and develop new clinical trial endpoints. Ionis has helped Biogen understand our antisense platform and the large potential of this powerful drug modality in neurological diseases," said Dr. C. Frank Bennett, senior vice president of Research and Franchise Leader for the Neurological Programs at Ionis. "Looking ahead, we are focused on continuing to advance Ionis' antisense technology and on creating an exciting stream of drugs for neurological diseases – both for Biogen and for our wholly-owned neurological disease portfolio."

The transaction is subject to customary closing conditions, including the expiration of the applicable waiting period under the Hart Scott Rodino Antitrust Improvements Act of 1976 in the United States.

Biogen and Ionis expect the deal to close in the second quarter of 2018. Stifel, Nicolaus & Company, Incorporated acted as exclusive financial advisor to Biogen in this transaction.

## CONFERENCE CALL AND WEBCAST

On April 20, 2018, at 8:15 a.m. Eastern Time, Biogen will host a live webcast and conference call to discuss the expanded collaboration with Ionis, which will be accessible through the Investors section of Biogen's website, [www.biogen.com](http://www.biogen.com). Supplemental information in the form of a slide presentation is also accessible at the same location on the internet and will be subsequently available on the website for at least one month.

On April 20, 2018, at 9:00 a.m. Eastern Time, Ionis will host a live webcast and conference call to discuss the expanded collaboration with Biogen. Interested parties may listen to the call by dialing 877-443-5662 or access the webcast at [www.ionispharma.com](http://www.ionispharma.com). A webcast replay will be available for a limited time at the same address.

## About Biogen

At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Kenneth Murray, and Nobel Prize winners Walter Gilbert and Phillip Sharp, and today has the leading portfolio of medicines to treat multiple sclerosis; has introduced the first and only approved treatment for spinal muscular atrophy; and is focused on advancing neuroscience research programs in Alzheimer's disease and dementia, multiple sclerosis and neuroimmunology, movement disorders, neuromuscular disorders, pain, ophthalmology, neuropsychiatry, and acute neurology. Biogen also manufactures and commercializes biosimilars of advanced biologics.

We routinely post information that may be important to investors on our website at [www.biogen.com](http://www.biogen.com). To learn more, please visit [www.biogen.com](http://www.biogen.com) and follow us on social media – [Twitter](#), [LinkedIn](#), [Facebook](#), [YouTube](#).

## 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 40 drugs in development. SPINRAZA® (nusinersen) has been approved in global markets for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Inotersen and volanesorsen are two antisense drugs that Ionis discovered and successfully advanced through Phase 3 studies. Inotersen is under regulatory review for marketing approval in the U.S. and EU for the treatment of patients with hereditary ATTR amyloidosis. Volanesorsen is under regulatory review for marketing approval in the U.S., EU, and Canada for the treatment of patients with familial chylomicronemia syndrome, or FCS. Volanesorsen is also in a Phase 3 study in patients with familial partial lipodystrophy, or FPL. Akcea Therapeutics, an affiliate of Ionis focused on developing and commercializing drugs to treat patients with serious and rare diseases, will commercialize inotersen and volanesorsen, if approved. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at [www.ionispharma.com](http://www.ionispharma.com).

## About SPINRAZA®

SPINRAZA is being developed globally for the treatment of SMA.

SPINRAZA is an antisense oligonucleotide (ASO), using Ionis Pharmaceutical Inc.'s proprietary antisense technology, that is designed to treat SMA caused by mutations or deletions in the SMN1 gene located in chromosome 5q that leads to SMN protein deficiency. SPINRAZA alters the splicing of SMN2 pre-mRNA in order to increase production of full-length SMN protein.<sup>1</sup> ASOs are short synthetic strings of nucleotides designed to selectively bind to target RNA and regulate gene expression. Through use of this technology, SPINRAZA has the potential to increase the amount of full-length SMN protein in individuals with SMA. SPINRAZA must be administered via intrathecal injection, which delivers therapies directly to the cerebrospinal fluid (CSF) around the spinal cord,<sup>2</sup> where motor neurons degenerate in individuals with SMA due to insufficient levels of SMN protein.<sup>3</sup>

SPINRAZA demonstrated a favorable benefit-risk profile. The most common adverse reactions reported for SPINRAZA were upper respiratory infection, lower respiratory infection, and constipation. Serious adverse reactions of atelectasis were more frequent in SPINRAZA-treated patients. Coagulation abnormalities and thrombocytopenia, including acute severe thrombocytopenia, have been observed after administration of some ASOs. Individuals may be at increased risk of bleeding complications. Renal toxicity has been observed after administration of some ASOs. SPINRAZA is present in and excreted by the kidney.

For additional important safety information, and the U.S. full prescribing information, please visit [www.spinraza.com](http://www.spinraza.com) or your respective country's website.

## Biogen Safe Harbor

This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to the potential benefits and results that may be achieved through Biogen's collaboration agreement with Ionis, risks and uncertainties associated with drug development and commercialization, the potential of Biogen's commercial business and pipeline programs, including potential novel antisense drug candidates for a broad range of neurological disease areas, including dementia, neuromuscular diseases, movement disorders, ophthalmology, diseases of the inner ear, and neuropsychiatry, the anticipated completion and timing of the transaction, and the potential benefits, safety, and efficacy of SPINRAZA. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "except," "forecast," "intend," "may," "plan," "potential," "possible," "will," and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation: risks that the transaction will be completed in a timely manner or at all; uncertainty as to whether the anticipated benefits and potential of Biogen's collaboration agreement with Ionis can be achieved; risks of unexpected costs or delays; uncertainty of success in the development and potential commercialization of novel antisense drug candidates for a broad range of neurological disease areas, including dementia, neuromuscular diseases, movement disorders, ophthalmology, diseases of the inner ear, and neuropsychiatry, which may be impacted by, among other things, the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of these drug candidates; Biogen and Ionis may encounter other unexpected hurdles which may be impacted by, among other things, the occurrence of adverse safety events, failure to

obtain regulatory approvals in certain jurisdictions, or failure to protect intellectual property and other proprietary rights; product liability claims; or third party collaboration risks. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this press release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments, or otherwise.

#### **IONIS' FORWARD-LOOKING STATEMENT**

This press release includes forward-looking statements regarding Ionis' collaboration with Biogen and the development, activity, therapeutic potential, commercial potential and safety of SPINRAZA, and the drugs in development for neurological diseases. 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, 2017, which is on file with the SEC. Copies of this and other documents are available from Ionis.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics™ is a trademark of Akcea Therapeutics, Inc. SPINRAZA® is a registered trademark of Biogen.

<sup>1</sup> Hua Y, Sahashi K, Hung G, Rigo F, Passini MA, Bennett CF, Krainer AR. Antisense correction of SMN2 splicing in the CNS rescues necrosis in a type III SMA mouse model. *Genes Dev.* 2010 Aug 1; 24(15):16344-44.

<sup>2</sup> Evers MM, Toonen LJ, van Roon-Mom WM. Antisense oligonucleotides in therapy for neurodegenerative disorders. *Adv Drug Deliv Rev.* 2015;87:90-103.

<sup>3</sup> Lunn MR, Wang CH. Spinal muscular atrophy. *Lancet.* 2008;371(9630):2120-2133.

View source version on businesswire.com: <https://www.businesswire.com/news/home/20180420005137/en/>

Source: Biogen

#### **Biogen**

##### **Media Contact:**

David Caouette, +1 617-679-4945

[public.affairs@biogen.com](mailto:public.affairs@biogen.com)

or

##### **Investor Contact:**

Matt Calistri, +1 781-464-2442

[IR@biogen.com](mailto:IR@biogen.com)

or

#### **Ionis Pharmaceuticals**

##### **Investor Contact:**

D. Wade Walke, Ph.D., 760-603-2741

Vice President, Corporate Communications and Investor Relations

or

##### **Media Contact:**

Amir Khan, 212-899-9730

[akhan@spectrumscience.com](mailto:akhan@spectrumscience.com)