Biogen Exercises Option with Ionis to Develop and Commercialize Investigational Treatment BIIB067 for a Subtype of Familial Amyotrophic Lateral Sclerosis (ALS) Based on Positive Phase 1 Data

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- Positive interim analysis demonstrated proof-of-biology and proof-of-concept for BIIB067
- Biogen plans to advance BIIB067 to a pivotal clinical study
- Biogen paid Ionis Pharmaceuticals a $35 million one-time upfront payment and may pay potential milestone payments and royalties

CAMBRIDGE, Mass. and CARLSBAD, Calif., Dec. 06, 2018 (GLOBE NEWSWIRE) -- Biogen Inc (Nasdaq: BIIB) and Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced today that Biogen exercised its option to obtain from Ionis a worldwide, exclusive, royalty-bearing license to develop and commercialize BIIB067 (IONIS-SOD1$_{RX}$), an investigational treatment for amyotrophic lateral sclerosis (ALS) with superoxide dismutase 1 (SOD1) mutations. ALS with SOD1 mutations is a subtype of familial ALS and accounts for approximately two percent of all ALS cases.

“Biogen and Ionis have a shared goal of bringing innovative therapies to those living with severe neurological diseases where there is significant unmet medical need,” said Michael Ehlers, M.D., Ph.D., executive vice president, research and development at Biogen. “The progress made to date in the BIIB067 clinical program is a positive step forward. We are committed to our goal of bringing forward a therapy for patients with ALS with SOD1 mutations, who currently have limited or no treatment options.”

The decision to exercise the option was based on a positive interim analysis of a randomized, placebo controlled single- and multiple-ascending dose Phase 1 study (n=70) that achieved proof-of-biology and proof-of-concept for BIIB067. At the highest dose tested (n=10), treatment with BIIB067 over a three month period resulted in a statistically significant lowering of SOD1 protein levels in the cerebrospinal fluid (p=0.002) and a numerical trend towards slowing of clinical decline as measured by the ALS Functional Rating Scale-Revised, both compared to placebo (n=12). The safety and tolerability profile in this analysis supports continued development of BIIB067 in ALS. Based on these results, Biogen plans to advance BIIB067 to a pivotal clinical study.

“The results from this study provide hope to SOD1 ALS patients who are suffering with this devastating disease,” said C. Frank Bennett, Ph.D., senior vice president of research and franchise leader for neurological programs at Ionis. “BIIB067 is the first investigational medicine targeting the known cause of this familial form of ALS to advance towards a pivotal study. Our broad strategic collaborations with Biogen have produced not only SPINRAZA, but six more drugs moving forward in development and a large number of preclinical and research programs. We believe our proprietary antisense technology will continue to bring benefit to patients now and in the future.”

As a part of the option exercise, Biogen made a one-time $35 million payment to Ionis. Future payments may include potential post-licensing milestone payments of up to $55 million and royalties in the low to mid-teen percentages on annual worldwide net sales. Biogen will be solely responsible for the costs and expenses related to the development, manufacturing and commercialization of BIIB067 following the option exercise.

ALS is a rare, fatal neurodegenerative disease characterized by motor neuron loss in the brain and spinal cord that are responsible for controlling voluntary muscle movement. Symptoms may vary depending on the location of the motor neuron failure and may include muscle stiffness and spasticity or spontaneous muscle twitching followed by atrophy. The average life expectancy for an ALS patient is less than five years from the time of diagnosis. Mutations within multiple genes are believed to cause ALS, including mutations in the SOD1 gene.

Final data results from the Phase 1 study are expected to be communicated at a future scientific forum.

About BIIB067
BIIB067 is an antisense oligonucleotide (ASO) RNase H-mediated inhibitor of SOD1 messenger ribonucleic acid (mRNA) being developed for the treatment of ALS with SOD1 mutations. BIIB067 binds to SOD1 mRNA, allowing its degradation by RNase-H and reducing protein production. This is thought to decrease the toxicity of mutant SOD1 and potentially provide therapeutic benefit through improved survival and function to people with ALS with SOD1 mutations. BIIB067 demonstrated proof-of-biology and proof-of-concept in a Phase 1 interim analysis. Biogen licensed BIIB067 from Ionis Pharmaceuticals under a collaborative development and license agreement.

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. To learn more, please visit www.biogen.com and follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

About Ionis Pharmaceuticals, Inc.
As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, proprietary antisense technology platform with the potential to treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs – such as children and adults with spinal muscular atrophy (SMA). We created SPINRAZA® (nusinersen)* and are proud to have brought new hope to the SMA community by developing the first and only approved treatment for this disease.

Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 drugs with the potential to treat patients with cardiovascular disease, rare diseases, neurological diseases, infectious diseases and cancer. We created TEGSEDI™ (inotersen) the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy of hereditary transthyretin (TTR) amyloidosis (ATTR) in adult patients that our affiliate Akcea Therapeutics is commercializing. Together with Akcea, we are also bringing new medicines to patients with cardiometabolic lipid disorders.

To learn more about Ionis follow us on twitter @ionispharma or visit http://ir.ionispharma.com/.

*SPINRAZA® is marketed by Biogen.

Biogen Safe Harbor Statement
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, including statements about results from the Phase 1 study of BIIB067; the potential clinical effects of BIIB067; the potential benefits, safety and efficacy of BIIB067; the identification and treatment of ALS; the potential of Biogen's commercial business and pipeline programs, including BIIB067; the anticipated benefits and potential of Biogen's collaboration arrangements with Ionis; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "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, uncertainty of success in the development and potential commercialization of BIIB067; the risk that Biogen may not fully enroll its clinical trials or enrollment will take longer than expected; unexpected concerns may arise from additional data, analysis or results obtained during Biogen's clinical trials; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen's drug candidates, including BIIB067; the occurrence of adverse safety events; the risks of other unexpected hurdles, costs or delays; failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; and 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 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 the therapeutic and commercial potential of Ionis' technologies and products in development, including BIIB067 (IONIS-SOD1$_{Rx}$), SPINRAZA® and TEGSEDI™ (inotersen). 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, and most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of this and other documents are available from the Company.

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