Biogen Announces Topline Results From Phase 2/3 Gene Therapy Study for XLRP

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- *While the Phase 2/3 XIRIUS study did not meet its primary endpoint, data indicated positive trends in several prespecified secondary endpoints, such as a clinically relevant measure of visual acuity*
- *Biogen will communicate next steps for the program after analyzing the complete data set*
- *Currently there are no approved treatments for X-linked retinitis pigmentosa (XLRP), a rare inherited retinal disease that ultimately leads to blindness in most people with the condition*

CAMBRIDGE, Mass., May 14, 2021 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced topline results from the Phase 2/3 XIRIUS study of cotoretigene toliparvovec (BIIB112), a gene therapy being investigated as a one-time therapy for patients with X-linked retinitis pigmentosa (XLRP). XLRP is a rare, inherited retinal disease that is associated with progressive vision loss as the light-sensing cells of the retina gradually deteriorate. Initial symptoms are difficulty seeing at night, followed by restriction of the field of vision and eventually blindness in most people by the age of 40. Patients living with XLRP currently have no approved treatments.

The XIRIUS study did not meet its primary endpoint of demonstrating a statistically significant improvement in the proportion of treated study eyes with ≥7 dB improvement from baseline at ≥5 of the 16 central loci of the 10-2 grid assessed by Macular Integrity Assessment (MAIA) microperimetry. This assessment was performed at 12 months and compared to the study eye of patients randomized to the untreated control group. Positive trends were observed across several clinically relevant prespecified secondary endpoints.

“Although the Phase 2/3 XIRIUS study of cotoretigene toliparvovec did not meet its primary endpoint, we are encouraged by positive trends in other pre-specified clinically relevant endpoints, such as a measure of visual acuity under low light conditions,” said Katherine Dawson, M.D., head of the therapeutics development unit at Biogen. “XLRP is a serious, early-onset form of retinitis pigmentosa, and people living with it face almost certain blindness by the end of the fourth decade, commonly leading to loss of independence, depression and unemployment. We are working to further evaluate the data from the XIRIUS study before communicating potential next steps for the cotoretigene toliparvovec clinical development program.”

Most adverse events were ocular in nature, mild-to-moderate in severity, and resolved.

Complete analysis of the XIRIUS study is ongoing, and detailed results will be shared in a future scientific forum.

Biogen is advancing its multi-franchise portfolio strategy by pursuing modalities including gene therapy to address significant unmet medical needs. In ophthalmology, in addition to cotoretigene toliparvovec, the company is currently evaluating the safety and efficacy of timrepigene emparvovec (BIIB111/AAV2-REP1), a gene therapy being investigated for the one-time treatment of choroideremia, a rare inherited retinal disease. The company also announced a global collaboration and licensing agreement with ViGeneron GmbH to develop and commercialize gene therapy products based on adeno-associated virus (AAV) vectors with the aim of treating inherited eye diseases as well as a licensing agreement with Massachusetts Eye and Ear to develop a gene therapy for the potential treatment of inherited retinal degeneration due to mutations in the *PRPF31* gene. In addition to Biogen’s gene therapy candidates for various ophthalmic conditions, the company also entered into an agreement with Catalyst Biosciences to develop and commercialize pegylated CB 2782 for the potential treatment of geographic atrophy, an advanced form of dry age-related macular degeneration that leads to blindness that has no approved therapies.

About Cotoretigene Toliparvovec
Cotoretigene toliparvovec (BIIB112) is an investigational AAV8 vector-based gene therapy administered by subretinal injection, designed to provide full-length functioning retinitis pigmentosa GTPase regulator (*RPGR*) protein in patients with X-linked retinitis pigmentosa (XLRP) caused by mutations in the *RPGR* gene.

By replacing the gene, cotoretigene toliparvovec leads to increased levels of the RPGR protein which may potentially slow, stop or prevent further degeneration of photoreceptors in patients with *RPGR*-associated XLRP.

About the XIRIUS Study (NCT03116113)
XIRIUS was a first-in-human, multicenter, randomized, three-arm dose-escalation and dose-expansion study of a single subretinal injection of cotoretigene toliparvovec in males with a genetically confirmed diagnosis of X-linked retinitis pigmentosa. Part I was a 24-month dose-escalation study (n=18, ≥18 years of age); Part II was a 12-month dose expansion study (n=32 randomized ≥10 years of age), with a high dose and low dose selected from Part I based on a benefit/risk assessment and a third untreated group to allow for a controlled comparison of efficacy and safety. At study completion, treated subjects in Parts I and II have been invited to participate in a separate long-term follow-up study that will collect efficacy and safety data up to five years from treatment.

For more information about the XIRIUS study, visit https://clinicaltrials.gov/.

About X-linked Retinitis Pigmentosa (XLRP)
X-linked retinitis pigmentosa (XLRP) is a rare, inherited retinal disease that is associated with progressive vision loss as the light-sensing cells of the retina gradually deteriorate, leading to blindness in most patients. XLRP primarily affects males and is caused most frequently by mutations in the retinitis pigmentosa GTPase regulator protein (*RPGR)* gene that result in the loss of photoreceptors, accumulation of retinal pigment deposits and eventual loss of vision. Typically beginning with night blindness in early adolescence, XLRP is an early-onset, severe form of retinitis pigmentosa. Approximately two to four males per 100,000 have a diagnosis of XLRP, and around 75 to 90 percent of XLRP cases with known genetic mutations are caused by *RPGR* gene mutations. Loss of sight can be devastating and lead to lost independence, unemployment, social isolation and depression.

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 as well as related therapeutic adjacencies. 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. Today Biogen has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for

spinal muscular atrophy, commercializes biosimilars of advanced biologics and is focused on advancing research programs in multiple sclerosis and neuroimmunology, Alzheimer's disease and dementia, neuromuscular disorders, movement disorders, ophthalmology, neuropsychiatry, immunology, acute neurology and neuropathic pain.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Biogen Safe Harbor Statement
This news 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, safety and efficacy of cotoretigene toliparvovec; the potential clinical effects of cotoretigene toliparvovec; results from the XIRIUS study of cotoretigene toliparvovec; the clinical development program, data readouts and presentations for cotoretigene toliparvovec; the treatment of XLRP; the potential of our commercial business and pipeline programs, including cotoretigene toliparvovec; the anticipated benefits and potential of our collaboration arrangements with ViGeneron GmbH, Massachusetts Eye and Ear and Catalyst Biosciences; our strategy and plans; 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," "would" 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 cotoretigene toliparvovec; unexpected concerns may arise from additional data, analysis or results obtained during the XIRIUS study; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including cotoretigene toliparvovec; the occurrence of adverse safety events; the risks of other unexpected hurdles, costs or delays; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; third party collaboration risks; and the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations and financial condition. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from our expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this news release. We do not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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