BioMarin, Pioneer in Phenylketonuria (PKU) Therapies, Submits Clinical Trial Application (CTA) in U.K. for Investigational Gene Therapy for PKU

BMN 307 Represents a Potential 3rd PKU Treatment Option in BioMarin's PKU Franchise
2nd Gene Therapy Program in Product Pipeline

SAN RAFAEL, Calif., Sept. 26, 2019 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (Nasdaq:BMRN), a pioneer in treatments for rare disease Phenylketonuria (PKU) and in gene therapies, today announced that it has submitted a Clinical Trial Application (CTA) with the Medicines and Healthcare Products Regulatory Agency (MHRA) in the U.K. for BMN 307, an investigational AAV5-phenylalanine hydroxylase (PAH) gene therapy designed to reduce blood phenylalanine (Phe) concentrations levels in patients with PKU. BMN 307 will be evaluated to determine whether a single dose of treatment can restore Phe metabolism in patients with PKU, normalize plasma Phe level, and enable a normal diet. The company expects to start enrolling patients in a Phase 1/2 trial early next year and is actively preparing regulatory submissions for other countries. BMN 307 represents a potential third PKU treatment option in BioMarin's PKU franchise and its second gene therapy development program. BMN 307 follows BioMarin's first investigational gene therapy program, valoctocogene roxaparvovec for severe hemophilia A, currently in a Phase 3 study.

"This clinical trial application marks the latest milestone in BioMarin's 15-plus year commitment to the PKU community. BioMarin has brought the only two approved therapies for PKU to patients around the world," said Hank Fuchs, President, Worldwide Research and Development at BioMarin. "Leveraging our expertise in gene therapy, we are pleased to be adding a new gene therapy product, which is potentially a transformative solution, to build on our current achievements for the PKU community."

PKU is a rare genetic disease that manifests at birth and is marked by an inability to break down Phe, an amino acid that is found in most forms of protein. Left untreated, high levels of Phe become toxic to the brain and may lead to serious neurological and neuropsychiatric-related issues, affecting the way a person thinks, feels, and acts. Due to the seriousness of these symptoms, in many countries, infants are screened at birth to ensure early diagnosis and treatment to avoid intellectual disability and other complications. According to treatment guidelines, PKU patients should maintain lifelong control of their Phe levels.

Phase 1/2 Study

The Phase 1/2 study will evaluate the safety efficacy and tolerability of a single intravenous administration of BMN 307 in patients with PKU. The Phase 1/2 study consists of a dose-escalation phase, followed by a dose expansion phase. In addition, there is also an observational study in PKU patients to measure markers of disease and clinical outcomes over time in patients.

BioMarin's 15-Plus Year Commitment to PKU Research

For more than 15 years, BioMarin has been a pioneer in ongoing research to help improve the lives of PKU patients. BioMarin has treated approximately 7,000 PKU patients around the world. The company has two approved PKU therapies, in addition to the investigational gene therapy BMN 307 in development. BioMarin has conducted 40 clinical studies in PKU and has sponsored 38 external clinical studies. BioMarin researchers have authored 54 publications in medical and scientific journals on PKU, and BioMarin has supported another 52 publications by external researchers.

About Gene Therapy

Gene therapy is a form of treatment designed to address a genetic problem by adding a corrected copy of the defective gene. The functional gene is inserted into a vector, containing a small DNA sequence, that acts as a delivery mechanism, providing the ability to deliver the functional gene to cells. The cells can then use the information to build the functional proteins that the body needs, potentially reducing or eliminating the cause of the disease.

Gene Therapy Manufacturing

BioMarin has constructed, commissioned, and validated one of the first gene therapy manufacturing facilities of its kind in the world, which is located in Novato, California. This facility can support up to 4,000 doses per year, and the production process was developed in accordance with International Conference on Harmonisation guidance to facilitate eventual worldwide registration with health authorities. In 2018, the International Society for Pharmaceutical Engineering (ISPE) selected the Company's gene therapy manufacturing facility as the Facility of the Year Category Winner for Project Execution. The BMN 307 PKU gene therapy clinical production occurred at commercial scale in this facility. Production of material at commercial scale in the state of the art facility significantly reduces risk associated with making process changes later in development and can speed overall development timelines.

About Phenylketonuria

PKU, or PAH deficiency, is a genetic disorder affecting approximately 50,000 diagnosed patients in the regions of the world where BioMarin operates and is caused by a deficiency of the enzyme PAH. This enzyme is required for the metabolism of Phe, an essential amino acid found in most protein-containing foods. If the active enzyme is not present in sufficient quantities, Phe accumulates to abnormally high levels in the blood and becomes toxic to the brain, resulting in a variety of complications including severe intellectual disability, seizures, tremors, behavioral problems and psychiatric symptoms. As a result of newborn screening efforts implemented in the 1960s and early 1970s, virtually all individuals with PKU under the age of 40 in countries with newborn screening programs are diagnosed at birth and treatment is implemented soon after. PKU can be managed with a Phe-restricted diet, which is supplemented by low-protein modified foods and Phe-free medical foods; however, it is difficult for most adult patients to adhere to the strict diet to the extent needed for achieving adequate control of blood Phe levels.

To learn more about PKU and PAH deficiency, please visit www.PKU.com. Information on this website is not incorporated by reference into this press release.

About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for patients with serious and life-threatening rare and ultra-rare genetic diseases. The company's portfolio consists of seven commercialized products and multiple clinical and pre-clinical product candidates. For additional information, please visit www.biomarin.com. Information on such website is not incorporated by reference into this press release.

Forward-Looking Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including, without limitation, statements about: the development of BioMarin's BMN 307 program generally, BioMarin's planned submissions to regulatory authorities for BMN 307, BioMarin's gene therapy manufacturing capabilities, and the timing and results of BioMarin's planned Phase 1/2 trial of BMN 307. These forward-looking statements are predictions and involve risks and uncertainties such that actual results may differ materially from these statements. These risks and uncertainties include, among others: results and timing of current and planned preclinical studies and clinical trials of BMN 307; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities; uncertainties inherent in research and development, including unfavorable new clinical data and additional analyses of existing clinical data; the results and timing of current and future clinical trials related to BMN 307; the risks related to commercialization of BMN 307 and our ability to manufacture sufficient quantities of BMN 307; and those factors detailed in BioMarin's filings with the Securities and Exchange Commission (SEC), including, without limitation, the factors contained under the caption "Risk Factors" in BioMarin's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 as such factors may be updated by any subsequent reports. Stockholders are urged not to place undue reliance on forward-looking statements, which speak only as of the date hereof. BioMarin is under no obligation, and expressly disclaims any obligation to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

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