BioMarin, Pioneer in Phenylketonuria (PKU) and Gene Therapy, Receives FDA Fast Track Designation for PKU Investigational Gene Therapy, BMN 307

2nd Investigational Gene Therapy in Clinic, Potential 3rd Therapy in PKU Franchise, 15+ Year Commitment to PKU Community

SAN RAFAEL, Calif., Oct. 2, 2020 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN), a pioneer in developing treatments for phenylketonuria (PKU) and gene therapies, announced today that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to BMN 307, an investigational gene therapy for the treatment of individuals with PKU.

Fast Track designation is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fulfill an unmet medical need, enabling drugs to reach patients earlier. Clinical programs with Fast Track designation may benefit from early and frequent communication with the FDA throughout the regulatory review process. These clinical programs may also be eligible to apply for Accelerated Approval and Priority Review if relevant criteria are met, as well as Rolling Review, which means that completed sections of the Biologic License Application can be submitted for review before the entire FDA application is complete. Both the FDA and European Medicines Agency have granted BMN 307 Orphan Drug Designation.

"Fast Track designation combined with our ability to conduct our clinical studies incorporating material manufactured using a commercial-ready process will further facilitate rapid clinical development of BMN 307 gene therapy," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "We are looking forward to working closely with the FDA, as well as other health agencies, to evaluate the safety and efficacy of this promising investigational gene therapy as we continue our unwavering 15-year commitment to advance the standard of care for people with PKU."

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 commonly found in many foods. Left untreated, high levels of Phe become toxic to the brain and may lead to serious neurological and neuropsychological issues, affecting a person's ability to think and problem solve, and can lead to depression, anxiety, and behavior disturbance impacting quality of life. 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.

BMN 307 Clinical Program

Last week, BioMarin announced that it had dosed the first participant in the global Phearless Phase 1/2 study with BMN 307, an AAV5-phenylalanine hydroxylase (PAH) gene therapy designed to normalize blood phenylalanine (Phe) concentration levels in patients with PKU by inserting a correct copy of the PAH gene into liver cells. BMN 307 will be evaluated to determine safety and whether a single dose of treatment can restore natural Phe metabolism, increase plasma Phe levels, and enable a normalization of diet in patients with PKU. BioMarin is conducting this study with material manufactured with a commercial-ready process to facilitate rapid clinical development and potentially support approval. BMN 307 represents a potential third PKU treatment option in BioMarin's PKU franchise and a second gene therapy development program.

BioMarin's clinical program is composed of two key studies. Phearless, a Phase 1/2 study, will evaluate the safety, efficacy, and tolerability of a single intravenous administration of BMN 307 in patients with PKU. The study consists of a dose-escalation phase, followed by a cohort expansion phase once an initially efficacious dose has been demonstrated. In addition, BioMarin is sponsoring an observational study, Phenom, which includes patients with PKU to measure both established and new markers of disease and clinical outcomes over time.

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 developed therapies that have been used to treat approximately 7,000 PKU patients around the world. The company has two approved PKU therapies, and the investigational gene therapy BMN 307 is currently in development. BioMarin has conducted 41 clinical studies in PKU and has sponsored 44 external clinical studies. BioMarin researchers have authored 65 publications in medical and scientific journals on PKU and supported another 57 publications by external researchers.

About Gene Therapy

Gene therapy is a form of treatment designed to address a genetic problem by adding a normal 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 targeted cells. The cells can then use the information from the normal gene to build the functional proteins that the body needs, potentially reducing or eliminating the cause of the disease.

Gene Therapy Manufacturing

BioMarin has leveraged its knowledge and experience in manufacturing complex biological products to design, construct and validate a state-of-the-art vector production facility in Novato, California. This facility is the site of production for both valoctocogene roxaparvovec and BMN 307, investigational gene therapies. Manufacturing capabilities are an essential driver for BioMarin's gene therapy programs and allows the Company to control quality, capacity, costs and scheduling enabling rapid development. Production of BMN 307 with a commercial ready process at scale reduces risk associated with making process changes later in development and may speed overall development timelines significantly.

Ongoing process development efforts and experience gained at commercial scale have led to improvements in productivity and operational efficiency. The ability to scale out the facility with additional equipment combined with the improvements in productivity result in a doubling of overall potential capacity to 10,000 doses per year, combined for both products, depending on final dose and product mix. This improvement in productivity is anticipated to meet potential commercial and clinical demand for both valoctocogene roxaparvovec and BMN 307 well into the future.

About Phenylketonuria

PKU, or phenylalanine hydroxylase (PAH) deficiency, is a genetic disorder affecting approximately 70,000 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 severe Phe-restricted diet, which is supplemented by low-protein modified foods and Phe-free medical foods; however, it is difficult for most patients to adhere to the life-long strict diet to the extent

needed to achieve adequate control of blood Phe levels. Dietary control of Phe in childhood can prevent major developmental neurological toxicities, but poor control of Phe in adolescence and adulthood is associated with a range of neurocognitive disabilities with significant functional impact.

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 six 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 Company's BMN 307 program being eligible to apply for Accelerated Approval and Priority Review if relevant criteria are met, as well as Rolling Review, the development of BioMarin's BMN 307 program generally, including the impact on the timing and process for regulatory interactions and decisions, BioMarin's gene therapy manufacturing capabilities and the anticipation that the current manufacturing capabilities will meet potential commercial and clinical demand for both valoctocogene roxaparvovec and BMN 307 well into the future and the impact of using material manufactured at commercial scale in a clinical trial on reducing risk and speeding up overall development timelines. 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: 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; our ability to reproducibly and consistently manufacture sufficient quantities of BMN 307, the possibility that changes may be required to the current manufacturing process; 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, 2020 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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