BioMarin, Pioneer in Phenylketonuria (PKU) and Gene Therapy, Doses First Participant in Global PHEARLESS Phase 1/2 Study of BMN 307 Gene Therapy

BioMarin Builds Upon 15+ Year Commitment to PKU Community with Potential 3rd Therapy in PKU Franchise

Company Leverages Gene Therapy Manufacturing Expertise Using Commercial-Ready Process

SAN RAFAEL, Calif., Sept. 24, 2020 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced today that it has dosed the first participant in the global PHEARLESS Phase 1/2 study with BMN 307, an investigational gene therapy for the treatment of individuals with PKU. BMN 307 is 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, normalize plasma Phe levels, and enable a normal diet in patients with PKU.

BioMarin will conduct 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.

"More than 70 years ago, the first child was treated for PKU in theUnited Kingdom at Birmingham Women's and Children's Hospital. Today, we continue to make strides in PKU treatment through the clinical study of a gene therapy for PKU," said Tarekegn G. Hiwot at University Hospitals Birmingham NHS Foundation Trust and principal investigator for the PHEARLESS study. "There is a tremendous unmet need for PKU patients. As a treating physician, it is important to me to be involved in clinical research to evaluate innovative therapies that have the potential to change the treatment paradigm in PKU for good."

"BioMarin has been committed to the PKU community for more than 15 years and remains dedicated to the research and development of innovative therapies to advance the standard of care for people with PKU," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "Building upon our experience of delivering two approved PKU therapies to the PKU community, BMN 307 gene therapy combines BioMarin's leadership in the development of PKU therapies with our expertise in gene

therapy development and manufacturing."

"PKU is a serious condition and many individuals struggle to manage their disorder on a daily basis. BioMarin is a pioneer in PKU treatments delivering the first two drug therapies to individuals with PKU. We applaud their unwavering commitment to drive research to bring a third treatment to the PKU community and for their substantial contributions to the overall body of scientific knowledge in PKU that they continue to make," said Christine S. Brown, MS, Executive Director, National PKU Alliance. "We are encouraged by BioMarin's efforts to develop a gene therapy that brings together their experience in PKU drug development, gene therapy development and gene therapy manufacturing. "

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 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.

Both the FDA and European Medicines Agency have granted BMN 307 Orphan Drug Designation. The Company is actively preparing regulatory submissions to open additional clinical sites in other countries.

BMN 307 Clinical 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 treated 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 that was cGMP certified by the EMA in Q2 2020. 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 both 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 development of BioMarin's BMN 307 program generally, BioMarin's planned submissions to regulatory authorities for BMN 307, BioMarin's gene therapy manufacturing capabilities, the impact of using material manufactured at commercial scale in a clinical trial, 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; 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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