BioMarin Announces First Patient Dosed in Phase 1/2 Study Evaluating Valoctocogene Roxaparvovec Gene Therapy in Severe Hemophilia A Patients with Pre-existing AAV5 Antibodies

SAN RAFAEL, Calif., May 15, 2018 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced today that it has dosed the first patient in a Phase 1/2 study (BMN 270-203) evaluating its investigational gene therapy, valoctocogene roxaparvovec, in severe hemophilia A patients with pre-existing AAV5 antibodies.

"Administration of valoctocogene roxaparvovec to this first patient seropositive for the AAV5 capsid is an important next step in our plan to expand the number and types of severe hemophilia A patients who may benefit from gene therapy and have antibodies to the vector," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "The goal with this study is to determine if patients that already have antibodies to AAV5 can be effectively treated with valoctocogene roxaparvovec. Our objective is to develop a therapy with the potential to eliminate the need for chronic treatment in severe hemophilia A across all patient sub-groups."

The study is an open-label, single-arm, titer-escalation trial evaluating the safety and efficacy of valoctocogene roxaparvovec in AAV5+ hemophilia A patients. Patients with pre-existing AAV5 antibodies will be sequentially enrolled into two titer cohorts that will encompass the range of observed AAV5 antibody titer levels generally observed in the hemophilia population and be treated with the 6e13 vg/kg dose. The primary endpoint will evaluate safety of valoctocogene roxaparvovec in this population. Secondary endpoints include assessment of FVIII activity level, frequency of required FVIII replacement therapy, and the number of bleeding episodes requiring treatment after therapy.

BioMarin is also evaluating the 6e13 vg/kg dose in GENEr8-1 and a second dose of 4e13 vg/kg in GENEr8-2, both global Phase 3 studies in patients without pre-existing AAV5 antibodies.

Regulatory Status
The U.S. Food and Drug Administration (FDA) granted valoctocogene roxaparvovec Breakthrough Therapy Designation. The FDA's Breakthrough Therapy Designation program is intended to facilitate and expedite development and review of new drugs to address unmet medical need in the treatment of a serious condition. To qualify for Breakthrough Therapy Designation, preliminary clinical evidence must show that that the drug may demonstrate substantial improvement over existing therapies.

The European Medicines Agency (EMA) has granted access to its Priority Medicines (PRIME) regulatory initiative for valoctocogene roxaparvovec. To be accepted for PRIME, an investigational therapy has to show its potential to benefit patients with unmet medical needs based on early clinical data. PRIME focuses on medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients with no treatment options. These medicines are considered priority medicines within the European Union (EU).

BioMarin's valoctocogene roxaparvovec has also received orphan drug designation from the FDA and EMA for the treatment of severe hemophilia A. The Orphan Drug Designation program is intended to advance the evaluation and development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions.

Gene Therapy Manufacturing
BioMarin has constructed one of the first gene therapy manufacturing facilities of its kind in the world, which is located in Novato, California. Good Manufacturing Practices (GMP) production of valoctocogene roxaparvovec has commenced and will support pivotal clinical development activities and anticipated commercial demand. This facility is capable of supporting approximately 2,000 to 3,000 patients per year, and the production process was developed in accordance with International Conference on Harmonisation guidance for Pharmaceuticals for Human Use facilitating worldwide registration with health authorities. Recently, the International Society for Pharmaceutical Engineering (ISPE) selected the company's gene therapy manufacturing facility as the 2018 Facility of the Year Category Winner for Project Execution.

About Hemophilia A
Hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation, a new mutation that was not inherited. Approximately 1 in 10,000 people is born with Hemophilia A. People living with the disease are not able to form blood clots efficiently and are at risk for excessive bleeding from modest injuries, potentially endangering their life. People with severe hemophilia often bleed spontaneously into their muscles or joints. The standard of care for the 43 percent of hemophilia A patients who are severely affected is a prophylactic regimen of Factor VIII infusions two to three times per week. Even with prophylactic regimens, many patients still experience spontaneous bleeding events that result in progressive and debilitating joint

damage.

About Gene Therapy
Gene therapy is a form of treatment designed to fix 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.

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.BMRN.com. Information on BioMarin's website is not incorporated by reference into this press release.

Forward-Looking Statements
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 valoctocogene roxaparvovec program generally; the potential benefit of valoctocogene roxaparvovec and of gene therapy generally for severe hemophilia A patients with pre-existing AAV5 antibodies and other patient sub-groups; the timing and results of the current and planned clinical trials of valoctocogene roxaparvovec; and BioMarin's gene therapy manufacturing facility, including its ability to support anticipated commercial demand of valoctocogene roxaparvovec, if approved. 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: timing and results of the current and planned clinical trials of valoctocogene roxaparvovec; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities; our ability to successfully manufacture the product candidate for the clinical trials, and if approved, for the anticipated commercial demand of valoctocogene roxaparvovec; and those other risks detailed from time to time under the caption "Risk Factors" and elsewhere in BioMarin's Securities and Exchange Commission (SEC) filings, including BioMarin's Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, and future filings and reports by BioMarin. BioMarin undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

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