

**BioMarin Provides Highlights of 4 Years of Clinical Data from Ongoing Phase 1/2 Study of Valoctocogene Roxaparvovec Gene Therapy for Severe Hemophilia A**

***All Study Participants Remain off Prophylactic Therapy***

***Cumulative Mean Annualized Bleed Rates Remain Less Than One (1) in Both 4e13 vg/kg (After 3 Years) and 6e13 vg/kg (After 4 Years) Dose Cohorts***

***Longest Duration of Clinical Experience for a Gene Therapy in Hemophilia A***

***Late-Breaking Abstract Submitted to Upcoming World Federation of Hemophilia Virtual Summit, June 14-19, 2020***

SAN RAFAEL, Calif., May 31, 2020 /[PRNewswire](#)/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced today an update to its previously reported results of an open-label Phase 1/2 study of valoctocogene roxaparvovec, an investigational gene therapy treatment for adults with severe hemophilia A.

The data have been submitted as a late-breaking abstract to the World Federation of Hemophilia (WFH) Virtual Summit to be held June 14-19, 2020.

The four-year update for the 6e13 vg/kg and three-year update for the 4e13 vg/kg cohorts demonstrated that all subjects in both cohorts remain off prophylactic Factor VIII treatment since receiving their single dose of valoctocogene roxaparvovec. Cumulative mean annualized bleed rates (ABR) remain less than one (1) in both cohorts and below pre-treatment baseline levels. The mean ABR in year four for the 6e13 vg/kg cohort was 1.3, and the mean ABR in year three for the 4e13 vg/kg cohort was 0.5. Over the past year, six of the seven participants in the 6e13 vg/kg cohort and five of the six

participants in the 4e13 vg/kg cohort remain free of spontaneous bleeds. Factor VIII activity levels declined commensurate with the most recent years' observations and remain in a range to provide hemostatic efficacy.

"It's been a privilege to participate in this pioneering research and to observe how the patients on the study have done so much to improve our understanding of gene therapy research for hemophilia A. This additional data is an important step toward a potential first treatment of its kind for this devastating disease," said Professor John Pasi, M.B., Ch.B., Ph.D., from Barts and the London School of Medicine and Dentistry; chief investigator for the valoctocogene roxaparvovec Phase 1/2 study, and a principal investigator for the Phase 3 study. "Each year of data increases our knowledge of safety and efficacy and contributes to the growing body of scientific data on gene therapies in general and hemophilia A in particular."

"BioMarin is proud to have advanced the community's knowledge of the potential for gene therapy to transform lives, and we are grateful for the support of the bleeding disorders community in this endeavor. In just over four years since starting clinical trials in patients, we've submitted applications for marketing authorizations globally, and we continue to contribute to the growing body of scientific data in gene therapy for hemophilia A with five studies underway," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "We continue to move forward with health authorities to make this treatment available for people with severe hemophilia A. We are committed to pioneering this field and advancing the standard of care for patients."

## **Safety Summary**

Overall, the safety profile of valoctocogene roxaparvovec remains consistent with previously reported data with no delayed-onset treatment related events.

No participants developed inhibitors to Factor VIII, and no participants withdrew from the study. No participants have developed thrombotic events. The most common adverse events associated with valoctocogene roxaparvovec occurred early and included transient infusion-associated reactions and transient, asymptomatic, and mild to moderate rise in the levels of certain proteins and enzymes measured in liver function tests with no long-lasting clinical sequelae.

## **Regulatory Status**

The Food and Drug Administration (FDA) is reviewing the biologics license application, under Priority Review, for valoctocogene roxaparvovec with a PDUFA action date of August 21, 2020. The FDA also granted valoctocogene roxaparvovec Breakthrough Therapy designation.

The European Medicines Agency (EMA) validated the Company's Marketing Authorization Application (MAA) for valoctocogene roxaparvovec which has been in review under accelerated assessment since January. Recognizing valoctocogene roxaparvovec for its potential to benefit patients with unmet medical needs, EMA granted access to its Priority Medicines (PRIME) regulatory initiative. Although the MAA remains under accelerated assessment at this time, the Company expects the review procedure to be extended by at least three months due to COVID-19 delays. Further, the Company believes there is a high possibility that the MAA will revert to the standard review procedure, as is the case with most filings that initially receive accelerated assessment. Because of the combination of these events, the Company expects an opinion from the Committee for Medicinal Products for Human Use (CHMP) in late 2020/early 2021.

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.

The Company believes that both submissions represent the first time a gene therapy product for any type of hemophilia indication is under review for marketing authorization by health authorities.

## **Gene Therapy Manufacturing**

The Company recently received EMA cGMP certification for its gene therapy manufacturing facility and quality systems for the production of valoctocogene roxaparvovec, an important step in obtaining regulatory approval of the product in the European Union. The Health Products Regulatory Authority (HPRA) of Ireland conducted, on behalf of EMA, a pre-approval inspection in the first quarter and issued a cGMP certification in the second quarter. The inspection of the facility by FDA is expected to be complete during the second quarter, which would allow for potential licensure of the facility in the U.S. consistent with the August 21st PDUFA date.

## **About Hemophilia A**

People living with hemophilia A lack sufficient functioning Factor VIII protein to help their blood clot and are at risk for painful and/or potentially life-threatening bleeds from even modest injuries. Additionally, people with the most severe form of hemophilia A (FVIII levels <1%) often experience painful, spontaneous bleeds into their muscles or joints. Individuals with the most severe form of hemophilia A make up approximately 50 percent of the hemophilia A population. People with hemophilia A with moderate (FVIII 1-5%) or mild (FVIII 5-40%) disease show a much-reduced propensity to bleed. The standard of

care for individuals with severe hemophilia A is a prophylactic regimen of replacement Factor VIII infusions administered intravenously up to two to three times per week or 100 to 150 infusions per year. Despite these regimens, many people continue to experience breakthrough bleeds, resulting in progressive and debilitating joint damage, which can have a major impact on their quality of life.

Hemophilia A, also called Factor VIII deficiency or classic hemophilia, is an X-linked 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 have Hemophilia A.

## **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.biomin.com](http://www.biomin.com). Information on BioMarin's 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., including without limitation, statements about: (i) the development of BioMarin's valoctocogene roxaparvovec program generally, (ii) the impact of valoctocogene roxaparvovec gene therapy for treating patients with severe hemophilia A, (iii) that Factor VIII activity levels declined commensurate with prior year's observations and

remain in a range to provide hemostatic efficacy, (iv) the planned updates of the Phase 1/2 study including the Company's submission of a late-breaking abstract to share four years of data at the WFH Virtual Summit, (v) the inspection of its gene therapy manufacturing facility by the FDA to be completed during the second quarter of 2020, (vi) the licensure of its gene therapy manufacturing facility, including the timing of such licensure, and (vii) the potential approval and commercialization of valoctocogene roxaparvovec for the treatment of severe hemophilia A, including timing of such approval decisions.

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 valoctocogene roxaparvovec, including final analysis of the above interim data; any potential adverse events observed in the continuing monitoring of the patients in the Phase 1/2 trial; the content and timing of decisions by the FDA, the European Commission and other regulatory authorities, including the potential impact of the COVID-19 pandemic on the regulatory authorities' abilities to issue such decisions and the timing of such decisions; the content and timing of decisions by local and central ethics committees regarding the clinical trials; BioMarin's ability to successfully manufacture 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, 2020, 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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