BioMarin Receives Complete Response Letter (CRL) from FDA for Valoctocogene Roxaparvovec Gene Therapy for Severe Hemophilia A

FDA Introduces New Recommendation for 2-Year Annualized Bleeding Rate (ABR) as Primary Endpoint for Ongoing Phase 3 Study 270-301

Company Committed to Working with FDA to Align on Next Steps to Obtain Approval

SAN RAFAEL, Calif., Aug. 19, 2020 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that the U.S. Food and Drug Administration (FDA) issued a Complete Response Letter (CRL) to the Company's Biologics License Application (BLA) for valoctocogene roxaparvovec gene therapy for severe hemophilia A on August 18, 2020. The FDA issues a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval in its present form.

Having previously agreed with the Agency on the extent of data necessary to support the BLA, the FDA introduced a new recommendation for two years of data from the Company's ongoing 270-301 study (Phase 3) to provide substantial evidence of a durable effect using Annualized Bleeding Rate (ABR) as the primary endpoint. The Agency first informed the Company of this recommendation in the CRL having not raised this at any time during development or review. The Agency recommended that the Company complete the Phase 3 Study and submit two-year follow-up safety and efficacy data on all study participants. FDA concluded that the differences between Study 270-201 (Phase 1/2) and the Phase 3 study limited its ability to rely on the Phase 1/2 study to support durability of effect. The Phase 3 study was fully enrolled in November 2019, and the last patient will complete two years of follow up in November 2021.

The Company plans to meet with the Agency in the coming weeks to align on the next steps to obtain approval.

"We remain committed to the hemophilia community and to leading the way to the first ever gene therapy in hemophilia A," said Jean-Jacques Bienaimé, Chairman and Chief Executive Officer of BioMarin. "We are surprised and disappointed that the FDA introduced new expectations for the first time in the Complete Response Letter. We are confident in valoctocogene roxaparvovec gene therapy and its potential to redefine the treatment paradigm for people with hemophilia A."

The application was based on the Phase 3 study interim analysis of study participants

treated with investigational product manufactured by the to-be-commercialized process and three-year data from the Phase 1/2 Study. The FDA had granted valoctocogene roxaparvovec Priority Review status and Breakthrough Therapy and Orphan Drug designations. Valoctocogene roxaparvovec maintains Breakthrough Therapy and Orphan Drug designations.

The ongoing valoctocogene roxaparvovec clinical trials will continue while BioMarin is exploring next steps to obtain approval. The European Medicines Agency (EMA) review of the Company's Marketing Authorization Application (MAA) for valoctocogene roxaparvovec is ongoing.

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 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 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., including without limitation, statements about: (i) the development of BioMarin's valoctocogene roxaparvovec program generally; (ii) further regulatory interactions with the FDA valoctocogene roxaparvovec: (iii) possible requirements for approval of valoctocogene roxaparvovec, including the suitability of Study 270-301 to meet such requirements; (iv) the conduct of ongoing clinical trials for valoctocogene roxaparvovec; (v) and the continued review of the Marketing Authorization Application for valoctocogene roxaparvovec by the European Medicines Agency. 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 the possible one year extension of Study 270-301; the content and timing of the expected follow up meeting with the FDA; the content and timing of decisions by the FDA, the European Commission and other regulatory authorities; 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 June 30, 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.

Contacts:

Investors	Media
Traci McCarty	*Debra Charlesworth*
BioMarin Pharmaceutical Inc.	*BioMarin Pharmaceutical Inc.*
(415) 455-7558	*(415) 455-7451*

SOURCE BioMarin Pharmaceutical Inc.
