BioMarin Announces Durable Hemostatic Efficacy Maintained Over 6 years in Ongoing Phase 1/2 Study of Valoctocogene Roxaparvovec, Investigational Gene Therapy for Hemophilia A

- 95% Reduction in Mean Annualized Bleed Rate (ABR) and 96% Reduction in Mean Annualized Factor VIII Usage from Baseline Through Year 6 in 6e13 vg/kg Dose Cohort
- 91% Reduction in Mean ABR and 93% Reduction in Mean Annualized Factor VIII Usage from Baseline Through Year 5 in 4e13 vg/kg Dose Cohort
- Data from Phase 1/2 Study to be Shared in Oral Presentation at Upcoming International Society on Thrombosis and Haemostasis (ISTH) 2022 Congress (July 9-13)
- BLA Resubmission Now Expected by End of September to Provide Additional Information Requested by FDA
- MAA Under Review by the European Medicines Agency (EMA), Opinion Anticipated Mid-year 2022

SAN RAFAEL, Calif., May 31, 2022 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced today updated results from its ongoing open-label Phase 1/2 study, which represents the longest duration of clinical observation for valoctocogene roxaparvovec, an investigational gene therapy treatment for adults with severe hemophilia A. The Company plans to share the data during an oral presentation at the upcoming International Society on Thrombosis and Haemostasis (ISTH) 2022 Congress (July 9-13). Six-year and five-year post-treatment follow-up of the 6e13 vg/kg and 4e13 vg/kg cohorts, respectively, demonstrated sustained hemostatic efficacy of valoctocogene

roxaparvovec.

6-Year Results in Phase 1/2 6e13 vg/kg Dose Cohort

All participants in the 6e13 vg/kg cohort remain off prophylactic Factor VIII treatment at the time of the data cut. The mean cumulative annualized bleed rate (ABR) remains less than one and substantially below baseline levels; the mean ABR in year six was 0.7 with a mean cumulative ABR reduction of 95% and Factor VIII use reduction of 96% through six years, compared to baseline.

5-Year Results in Phase 1/2 4e13 vg/kg Dose Cohort

All participants in the 4e13 vg/kg cohort were off prophylactic Factor VIII at the time of the data cut. Six months prior to the data cut, one participant temporarily resumed prophylactic Factor VIII treatment for one month, after which he was bleed free through the last follow up. The mean ABR in year five for the 4e13 vg/kg cohort was 0.7 with a mean cumulative ABR reduction of 91% and Factor VIII use reduction of 93% through five years, compared to baseline.

The trajectory of Factor VIII activity levels in both the 6e13 vg/kg and 4e13 vg/kg cohorts were commensurate with the most recent years' observations.

"With every year of observation in this study, we learn more about the impact of a single infusion of valoctocogene roxaparvovec on hemostatic control and continue to see low levels of bleeds in the absence of prophylactic therapy," said Professor Michael Laffan, faculty of Medicine, Department of Immunology and Inflammation at Imperial College London, Director of the Hammersmith Hospital Haemophilia Centre, and Chief Investigator for the valoctocogene roxaparvovec Phase 1/2 study. "Six years of data represents the longest duration of clinical experience for a gene therapy in Hemophilia A and provides

unparalleled understanding of safety."

"We continue to work with regulatory authorities to potentially make available the first gene therapy in severe hemophilia A as an important treatment option. The thorough feedback recently provided by the FDA increases our ability to support the FDA's review of our application and hopefully makes Roctavian available as a choice for patients in the United States," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "We are encouraged after six years of data in this Phase 1/2 study by the consistent and durable bleed control following a one-time treatment with valoctocogene roxaparvovec. These data demonstrate the potential to change the treatment paradigm by providing severe hemophilia A patients hope for longer intervals free from prophylactic therapy."

Regulatory Status

BioMarin plans to include the previously reported results from the two-year follow-up safety and efficacy data from the Phase 3 GENEr8-1 study in a Biologics Licensing Application (BLA) resubmission for valoctocogene roxaparvovec to the Food and Drug Administration (FDA). Based on recent feedback received from the FDA related to BioMarin's plans for the upcoming BLA, the Agency has requested additional information and analyses of data to be included in the BLA prior to submission. The FDA has not requested additional pre-clinical or clinical studies. While at present, no requests have been made concerning evaluation of efficacy and safety three years after dosing from the GENEr8-1 study, BioMarin is aware that such data will become available during the anticipated BLA review. Based on these new information requests, the BLA resubmission is now expected by the end of September.

The FDA granted Regenerative Medicine Advanced Therapy (RMAT)

designation to valoctocogene roxaparvovec in March 2021. RMAT is an expedited program intended to facilitate development and review of regenerative medicine therapies, such as valoctocogene roxaparvovec, that are intended to address an unmet medical need in patients with serious conditions. The RMAT designation is complementary to Breakthrough Therapy Designation, which the Company received in 2017.

In addition to the RMAT Designation and Breakthrough Therapy Designation, BioMarin's valoctocogene roxaparvovec also has 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 European Medicines Agency (EMA) continues the review of BioMarin's Marketing Authorization Application (MAA) for valoctocogene roxaparvovec, and we anticipate a Committee for Medicinal Products for Human Use (CHMP) opinion mid-year 2022. BioMarin has provided the EMA with two-year follow-up safety and efficacy data from the GENEr8-1 study.

Safety Summary

Overall, the safety profile of valoctocogene roxaparvovec in the Phase 1/2 study remains consistent with previously reported data with no delayed-onset treatment related adverse events. All participants continue to remain off corticosteroids since the first year. 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 after a single infusion and included short-lived 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.

A Serious Adverse Event of a parotid acinic cell carcinoma was identified in one study participant, who was treated more than five years ago, and was reported as unrelated to valoctocogene roxaparvovec by the investigator. The study participant was successfully treated. The relevant health authorities were notified, and all studies remain ongoing without modification. The independent Data Monitoring Committee (DMC) further reviewed the case. A genomic analysis was conducted as prespecified in the clinical trial protocol and the findings from the completed analysis showed a comparable pattern of integration between healthy and tumor containing tissues, with no evidence emerging that vector integration contributed to the salivary gland mass.

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 people with serious and life-threatening rare diseases and medical conditions. The Company selects product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market or offer a significant benefit over existing products. The Company's portfolio consists of seven commercial products and multiple clinical and preclinical product candidates for the treatment of various diseases. For additional information, please visit www.biomarin.com.

Forward-Looking Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc., including without limitation, statements about: the six-year and five-year post-treatment follow-up of the 6e13 vg/kg and 4e13 vg/kg cohorts in the Phase 1/2 study, respectively, demonstrated sustained hemostatic efficacy of valoctocogene roxaparvovec; the potential to change the treatment paradigm by providing severe hemophilia A patients hope for longer intervals free from prophylactic therapy; the trajectory of Factor VIII activity levels in both the 6e13 vg/kg and 4e13 vg/kg cohorts being commensurate with the most recent years' observations; the development of BioMarin's valoctocogene roxaparvovec program generally; the impact of valoctocogene roxaparvovec gene therapy for treating patients with

severe hemophilia A; the planned updates of the Phase 1/2 study including the Company's upcoming oral presentation of the data at ISTH 2022; the Company's plans to include the previously reported results from the two-year follow-up safety and efficacy data from the Phase 3 GENEr8-1 study in a BLA; the timing of the expected BLA resubmission by the end of September in order to provide additional information requested by FDA; the thorough feedback recently provided by the FDA increasing the Company's ability to support the FDA's review of the BLA and hopefully make Roctavian available as a treatment choice for patients in the United States; the anticipated CHMP opinion mid-year 2022; 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 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, 2022, and future filings and reports by BioMarin. Stockholders are urged not to place undue reliance on forward-looking statements, which speak only as of the date hereof. 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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Contacts:

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

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