BioMarin Announces First Person Treated Commercially with ROCTAVIAN® (valoctocogene roxaparvovec-rvox) for Severe Hemophilia A in Europe

First Person Treated in Germany; Reimbursement Discussions on Track in France and Italy

In the U.S., ROCTAVIAN Now Commercially Available and Hemophilia Treatment Centers Have Begun Screening Eligible Individuals

SAN RAFAEL, Calif., Aug. 30, 2023 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (Nasdaq: BMRN), a global biotechnology company dedicated to transforming lives through genetic discovery, today announced that an individual in Germany with severe hemophilia A was treated with ROCTAVIAN® (valoctocogene roxaparvovec-rvox), marking the first time that the gene therapy has been given commercially in Europe.

"Today represents an important milestone for the hemophilia community, and for patients and physicians around the world seeking access to ROCTAVIAN," said Jeff Ajer, executive vice president and chief commercial officer at BioMarin. "We look forward to more people gaining access to ROCTAVIAN in the rest of Europe, as well as the United States, where ROCTAVIAN recently received FDA approval."

Hemophilia treatment centers (HTCs) in Germany are testing people with hemophilia to determine treatment eligibility for the one-time gene therapy. Before beginning treatment, individuals are evaluated clinically and undergo testing. Currently, dozens of individuals are undergoing screening to determine eligibility for treatment with ROCTAVIAN. Final federal price negotiations in Germany are also ongoing.

"The burden of severe hemophilia A for people who are living with the condition is substantial, and there remains a significant unmet need for effective treatments that do not require chronic therapy. This one-time infusion represents an important milestone, offering new hope and potential, for eligible individuals in Germany," said PD Dr. med. Robert Klamroth, a treating physician and chief physician of the Center for Hemophilia and Hemostaseology at the Vivantes Klinikum in Berlin, Germany. "Bringing this therapy to all those who can benefit is critical to improve outcomes for individuals with severe hemophilia A."

Beyond Germany, the company's applications seeking price and reimbursement

approvals and other launch preparation activities continue to progress in France and Italy. In Italy, ROCTAVIAN was awarded conditional innovation designation, which is expected to facilitate pricing and reimbursement.

U.S. Launch Activities Accelerating, including Eligibility Testing at HTCs

In June, the FDA approved ROCTAVIAN for the treatment of adults with severe hemophilia A (congenital factor VIII (FVIII) deficiency with FVIII activity < 1 IU/dL) without antibodies to adeno-associated virus serotype 5 (AAV5) detected by an FDA-approved test.

ROCTAVIAN is now commercially available in the U.S. and HTCs have begun screening people with severe hemophilia A to determine eligibility. BioMarin has also seen an increasing inflow of patient consent forms and a number of executed or in-process warranty agreements that are expected to facilitate access and uptake of ROCTAVIAN at HTCs across the U.S.

About Hemophilia A

Hemophilia A, also called FVIII deficiency or classic hemophilia, is an X-linked genetic disorder caused by missing or defective FVIII, a clotting protein. Although it is passed down from parents to children, about one-third of cases are caused by a spontaneous mutation, a new mutation that was not inherited. Approximately 1 in 10,000 people have hemophilia A.

People living with hemophilia A lack sufficient functioning FVIII 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% of the hemophilia A population. People with hemophilia A with moderate (FVIII levels 1-5%) or mild (FVIII levels 5-40%) disease show a much-reduced propensity to bleed. Individuals with severe hemophilia A are treated with a prophylactic regimen of intravenous FVIII infusions administered 2-3 times per week (100-150 infusions per year) or a bispecific monoclonal antibody that mimics the activity of FVIII administered 1-4 times per month (12-48 injections or shots 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.

About ROCTAVIAN

ROCTAVIAN is an adeno-associated virus vector–based gene therapy indicated for the treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) without antibodies to adeno–associated virus serotype 5 (AAV5) detected by an FDA–approved test. The one-time infusion works by delivering a functional gene that is designed to enable the body to produce FVIII on its own, reducing the need for ongoing prophylaxis, demonstrated by results reported through a 3-year study period.

The European Commission (EC) granted conditional marketing authorization to ROCTAVIAN on August 24, 2022.

More information on testing to determine eligibility to receive ROCTAVIAN can be found at https://www.ROCTAVIAN.com in the U.S. and https://www.ROCTAVIAN.de in Germany.

U.S. Important Safety Information

Contraindications: Patients with active infections, either acute (such as acute respiratory infections or acute hepatitis) or uncontrolled chronic (such as chronic active hepatitis B). Patients with known significant hepatic fibrosis (stage 3 or 4 on the Batts-Ludwig scale or equivalent), or cirrhosis, and patients with known hypersensitivity to mannitol.

Infusion-related reactions including hypersensitivity reactions and anaphylaxis, have occurred. Monitor during and for at least 3 hours after ROCTAVIAN administration. Administer ROCTAVIAN in a setting where personnel and equipment are immediately available to treat infusion-related reactions. Discontinue infusion for anaphylaxis.

Hepatotoxicity: The safety and effectiveness of ROCTAVIAN in patients with hepatic impairment has not been established. Perform liver health assessments prior to administration. The majority of patients treated with ROCTAVIAN experienced ALT elevations and required corticosteroids for ALT elevation. Assess patient's ability to receive corticosteroids and/or other immunosuppressive therapy that may be required for an extended period. Live vaccines should not be administered to patients while on immunosuppressive therapy.

Monitor ALT weekly for at least 26 weeks and as clinically indicated, during corticosteroid therapy and institute corticosteroid treatment in response to ALT elevations as required. Continue to monitor ALT until it returns to baseline. Monitor factor VIII activity levels since ALT elevation may be accompanied by a decrease in factor VIII activity. One case

of autoimmune hepatitis was reported during third year follow-up in a patient with history of hepatitis C and steatohepatitis.

It is recommended that patients abstain from consuming alcohol for at least 1 year after administration and thereafter limit alcohol use. Concomitant medications may cause hepatotoxicity, decrease factor VIII activity, or change plasma corticosteroid levels which may impact liver enzyme elevation and/or factor VIII activity or decrease the efficacy of the corticosteroid regimen or increase their side effects. Closely monitor concomitant medication use including herbal products and nutritional supplements and consider alternative medications in case of potential drug interactions.

Thromboembolic events: Factor VIII activity above ULN has been reported following ROCTAVIAN infusion. Thromboembolic events may occur in the setting of elevated factor VIII activity above ULN. Evaluate patients for risk of thrombosis including general cardiovascular risk factors before and after administration of ROCTAVIAN. Advise patients on their individual risk of thrombosis in relation to their factor VIII activity levels above ULN and consider prophylactic anticoagulation. Advise patients to seek immediate medical attention for signs or symptoms indicative of a thrombotic event.

Factor VIII inhibitors and Monitoring for inhibitors: The safety and effectiveness of ROCTAVIAN in patients with prior or active factor VIII inhibitors have not been established. Patients with active factor VIII inhibitors should not take ROCTAVIAN. Following administration, monitor patients for factor VIII inhibitors (neutralizing antibodies to factor VIII). Test for factor VIII inhibitors especially if bleeding is not controlled, or plasma factor VIII activity levels decrease.

Monitor Factor VIII using the same schedule for ALT monitoring. It may take several weeks after ROCTAVIAN infusion before ROCTAVIAN-derived factor VIII activity rises to a level sufficient for prevention of spontaneous bleeding episodes. Exogenous factor VIII or other hemostatic products may also be required in case of surgery, invasive procedures, trauma, or bleeds. Consider more frequent monitoring in patients with factor VIII activity levels ≤ 5 IU/dL and evidence of bleeding, taking into account the stability of factor VIII levels since the previous measurement.

Factor VIII activity produced by ROCTAVIAN in human plasma is higher if measured with one-stage clotting assays compared to chromogenic substrate assays. When switching from hemostatic products prior to ROCTAVIAN treatment, physicians should refer to the relevant prescribing information to avoid the potential for factor VIII activity assay interference during the transition period.

Malignancy: The integration of liver-targeting AAV vector DNA into the genome may carry the theoretical risk of hepatocellular carcinoma development. ROCTAVIAN can also insert into the DNA of other human body cells. Monitor patients with risk factors for hepatocellular carcinoma (e.g., hepatitis B or C, non-alcoholic fatty liver disease, chronic alcohol consumption, non-alcoholic steatohepatitis, advanced age) with regular liver ultrasound (e.g., annually) and alpha-fetoprotein testing for 5 years following ROCTAVIAN administration. In the event that any malignancy occurs after treatment with ROCTAVIAN, contact BioMarin Pharmaceutical Inc. at 1-866-906-6100.

Most Common Adverse Reactions: Most common adverse reactions (incidence ≥ 5%) were nausea, fatigue, headache, infusion-related reactions, vomiting, and abdominal pain. Most common laboratory abnormalities (incidence ≥ 10%) were ALT, AST, LDH, CPK, factor VIII activity levels, GGT and bilirubin > ULN. Patients also experienced adverse reactions from corticosteroid use.

Isotretinoin, Efavirenz, and HIV Positive Patients: Isotretinoin is not recommended in patients who are benefiting from ROCTAVIAN. Efavirenz is not recommended in patients treated with ROCTAVIAN. Clinical studies of ROCTAVIAN did not include sufficient numbers of patients with HIV to determine whether the efficacy and safety differs compared to patients without HIV infection.

Females and Males of Reproductive Potential: ROCTAVIAN is not intended for administration in women. There are no data on the use of ROCTAVIAN in pregnant women or regarding lactation. For 6 months after administration of ROCTAVIAN, men of reproductive potential and their female partners must prevent or postpone pregnancy using an effective form of contraception, and men must not donate semen.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to BioMarin at 1-866-906-6100.

Please see the ROCTAVIAN full Prescribing Information for additional Important Safety Information.

About BioMarin

Founded in 1997, BioMarin is a global biotechnology company dedicated to transforming lives through genetic discovery. The company develops and commercializes targeted therapies that address the root cause of genetic conditions. BioMarin's unparalleled research and development capabilities have resulted in eight transformational

commercial therapies for patients with rare genetic disorders. The company's distinctive approach to drug discovery has produced a diverse pipeline of commercial, clinical, and pre-clinical candidates that address a significant unmet medical need, have well-understood biology, and provide an opportunity to be first-to-market or offer a substantial benefit over existing treatment options. For additional information, please visit www.biomarin.com.

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 potential impact of the first commercial treatment with ROCTAVIAN for severe hemophilia A in Europe, including (i) the potential benefits for the hemophilia community, and patients and physicians in Germany and around the world seeking access to ROCTAVIAN, (ii) BioMarin's ability to commercially progress ROCTAVIAN in Europe and the United States, and (iii) ROCTAVIAN's ability to improve outcomes for individuals with severe hemophilia A; the commercialization of ROCTAVIAN, including (i) BioMarin's expectations regarding the number of patients who will be eligible to receive ROCTAVIAN, including through patient eligibility testing at HTCs in Germany and the United States, (ii) BioMarin's expectations regarding the ability to facilitate access and uptake of ROCTAVIAN at HTCs across the United States, and (iii) BioMarin's ability to obtain price and reimbursement approvals in Germany, France and Italy; and the clinical development of BioMarin's comprehensive gene therapy program for the treatment of severe hemophilia A, including the ongoing clinical development of ROCTAVIAN. 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: BioMarin's success in the commercialization of ROCTAVIAN, including achieving adequate market share and reimbursement levels; whether ROCTAVIAN will have the impacts and benefits as anticipated; the results and timing of current and planned preclinical studies and clinical trials of ROCTAVIAN and the release of data from those trials, including continued monitoring of the participants in the clinical trials and post-approval studies; BioMarin's ability to successfully manufacture ROCTAVIAN for the clinical trials and commercially; the content and timing of decisions by the FDA, EU health authorities and other regulatory authorities regarding ROCTAVIAN; 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, 2023, 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.

BioMarin® is a registered trademark of BioMarin Pharmaceutical Inc. ROCTAVIAN® is a trademark of BioMarin Pharmaceutical Inc., with registration in Europe and pending in the U.S.

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