BioMarin Receives Positive CHMP Opinion in Europe to Expand Use of VOXZOGO® (vosoritide) to Treat Children Aged 4 Months and Older with Achondroplasia

European Commission Approval Decision Expected Q4 2023

Opinion Based on Positive Results from Global Phase 2 and Ongoing Extension Study

U.S. Food and Drug Administration PDUFA Target Action Date for Supplemental New Drug Application for VOXZOGO for Children Under 5 is Oct. 21, 2023

SAN RAFAEL, Calif., Sept. 15, 2023 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (Nasdaq: BMRN), a global biotechnology company dedicated to transforming lives through genetic discovery, today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending marketing authorization to expand the indication for VOXZOGO® (vosoritide) for injection to treat children with achondroplasia aged 4 months and older whose epiphyses (growth plates) are not closed. The diagnosis of achondroplasia should be confirmed by appropriate genetic testing. A final approval decision, typically consistent with the CHMP recommendation, is expected from the European Commission in the fourth quarter of 2023. VOXZOGO is currently approved in Europe in children with achondroplasia who are 2 years of age and older with open growth plates.

The U.S. Food and Drug Administration (FDA) has also set a PDUFA Target Action Date of Oct. 21, 2023, for the company's Supplemental New Drug Application (sNDA) for VOXZOGO to expand treatment in the United States to include children with achondroplasia under the age of 5 years. VOXZOGO is currently approved in the U.S. in children with achondroplasia who are 5 years of age and older with open growth plates.

"The expansion of VOXZOGO to allow physicians to begin treatment earlier offers the possibility of increased growth and other potential important long-term benefits," said Hank Fuchs, M.D., president of Worldwide Research and Development at BioMarin. "We look forward to the final approval decision from the European Commission, as well as a decision from the FDA, later this year. These approvals have the potential to further advance care by reaching very young children with achondroplasia."

Since the introduction of VOXZOGO in 2021, the company has seen strong demand for

the medicine worldwide. Over the last few weeks, BioMarin has increased fill-finish commitments and is continuing to work with the company's fill-finish provider to meet additional demand.

VOXZOGO is the only approved treatment that addresses the underlying cause of achondroplasia. The CHMP based its opinion on data and outcomes from the randomized, double-blind, placebo-controlled Phase 2 clinical trial (111-206) in children aged 4 months to 5 years that showed an improvement in height Z-score of approximately 0.3 standard deviations (SDS) across all age groups after one year of treatment. The application also included longer-term data from the ongoing extension study (111-208).

"For the first time, very young children with achondroplasia may have access to a treatment that has the potential to address the root cause of the condition," said Klaus Mohnike, professor of pediatrics at Magdeburg University Hospital in Germany and investigator for the VOXZOGO clinical program. "This is a remarkable step forward in our approach to treating achondroplasia."

VOXZOGO Safety

The safety profile was generally consistent with that seen in older participants in the Phase 3 VOXZOGO 301 study (the current label population in the U.S.). The most common adverse events were mild and self-limiting injection site reactions. See the U.S. Important Safety Information below and full Prescribing Information and the EU (European Union) Summary of Product Characteristics for additional safety information.

Description of Phase 2 Study in Infants and Toddlers

The 52-week phase 2 study enrolled 75 infants and young children with achondroplasia, aged zero to less than five years old (60 months). The study consisted of three cohorts by age (24 months to less than 5 years, 6 months to less than 24 months, less than 6 months) and was followed by a subsequent open-label extension trial where all children received active treatment. The objectives of the study were to evaluate safety, tolerability, and the effect of VOXZOGO on growth. The study also evaluated proportionality, functionality, quality of life, sleep apnea, and foramen magnum dimension, as well as the advent of major illnesses and surgeries which frequently occur in children with achondroplasia.

About VOXZOGO® (vosoritide) for Injection

In individuals with achondroplasia, endochondral bone growth, an essential process by which bone tissue is created, is negatively regulated due to a gain of function mutation in fibroblast growth factor receptor 3 gene (*FGFR3*). VOXZOGO, a C-type natriuretic peptide

(CNP) analog, represents a new class of therapy, which acts as a positive regulator of the signaling pathway downstream of FGFR3 to promote endochondral bone growth.

Through BioMarin's broad clinical development program, the company has enrolled 250 children with achondroplasia from eight countries in seven clinical studies evaluating the safety and efficacy of VOXZOGO.

VOXZOGO is currently approved in Europe in children with achondroplasia who are 2 years of age and older with open growth plates.

VOXZOGO is also approved in the U.S. and indicated to increase linear growth in children with achondroplasia who are 5 years of age and older with open growth plates. This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). To fulfill this post-marketing requirement, BioMarin intends to use the ongoing open-label extension studies compared to available natural history.

About Achondroplasia

Achondroplasia, the most common form of skeletal dysplasia leading to disproportionate short stature in humans, is characterized by slowing of endochondral ossification, which results in disproportionate short stature and disordered architecture in the long bones, spine, face, and base of the skull. This condition is caused by a change in the fibroblast growth factor receptor 3 gene (FGFR3), a negative regulator of bone growth.

More than 80% of children with achondroplasia have parents of average stature and have the condition as the result of a spontaneous gene mutation. The worldwide incidence rate of achondroplasia is about one in 25,000 live births. VOXZOGO is being tested in children whose growth plates are still "open," typically those under 18 years of age. Approximately 25% of people with achondroplasia fall into this category.

U.S. FDA-Approved Indication

VOXZOGO is a C type natriuretic peptide (CNP) analog indicated to increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses. This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

VOXZOGO U.S. Important Safety Information

What is VOXZOGO used for?

- VOXZOGO is a prescription medicine used to increase linear growth in children with achondroplasia who are 5 years of age and older with open growth plates (epiphyses).
- It is not known if VOXZOGO is safe and effective in children with achondroplasia under 5 years of age.
- VOXZOGO is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

What is the most important safety information about VOXZOGO?

- VOXZOGO may cause serious side effects including a temporary decrease in blood pressure in some patients. To reduce the risk of a decrease in blood pressure and associated symptoms (dizziness, feeling tired, or nausea), patients should eat a meal and drink 8 to 10 ounces of fluid within 1 hour before receiving VOXZOGO.

What are the most common side effects of VOXZOGO?

- The most common side effects of VOXZOGO include injection site reactions (including redness, itching, swelling, bruising, rash, hives, and injection site pain), vomiting, joint pain, decreased blood pressure, and stomachache. These are not all the possible side effects of VOXZOGO. Ask your healthcare provider for medical advice about side effects, and about any side effects that bother the patient or that do not go away.

How is VOXZOGO taken?

- VOXZOGO is taken daily as an injection given under the skin, administered by a caregiver after a healthcare provider determines the caregiver is able to administer VOXZOGO. Do not try to inject VOXZOGO until you have been shown the right way by your healthcare provider. VOXZOGO is supplied with Instructions for Use that describe the steps for preparing, injecting, and disposing VOXZOGO. Caregivers should review the Instructions for Use for guidance and any time they receive a refill of VOXZOGO in case any changes have been made.
- Inject VOXZOGO 1 time every day, at about the same time each day. If a dose of VOXZOGO is missed, it can be given within 12 hours from the missed dose. After

12 hours, skip the missed dose and administer the next daily dose as usual.

- The dose of VOXZOGO is based on body weight. Your healthcare provider will adjust the dose based on changes in weight following regular check-ups.
- Your healthcare provider will monitor the patient's growth and tell you when to stop taking VOXZOGO if they determine the patient is no longer able to grow. Stop administering VOXZOGO if instructed by your healthcare provider.

What should you tell the doctor before or during taking VOXZOGO?

- Tell your doctor about all of the patient's medical conditions including
    - If the patient has heart disease (cardiac or vascular disease), or if the patient is on blood pressure medicine (anti-hypertensive medicine).
    - If the patient has kidney problems or renal impairment.
    - If the patient is pregnant or plans to become pregnant. It is not known if VOXZOGO will harm the unborn baby.
    - If the patient is breastfeeding or plans to breastfeed. It is not known if VOXZOGO passes into breast milk.

- Tell your doctor about all of the medicines the patient takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

You may report side effects to BioMarin at 1-866-906-6100. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see additional safety information in the full Prescribing Information and Patient 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 the 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 development of BioMarin's VOXZOGO program, including (i) BioMarin's expectations regarding timing and the ability to obtain final approval decision from the European Commission for the marketing authorization to expand the indication for VOXZOGO, and (ii) BioMarin's expectations regarding the PDUFA Target Action Date with respect to its sNDA for VOXZOGO to expand treatment in the United States to include children with achondroplasia under the age of 5 years; the potential impact of obtaining final approvals for expanded indications from the European Commission and the FDA, including BioMarin's expectations regarding the number of additional children with achondroplasia that could be prescribed with VOXZOGO and related potential benefits; the potential benefits of VOXZOGO for children with achondroplasia, including the duration of such benefits and potential improvement in proportionality; and the continued clinical development of VOXZOGO. 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 VOXZOGO; any potential adverse events observed in the continuing monitoring of the patients in the clinical trials; the content and timing of decisions by the FDA, the EMA, the European Commission and other regulatory authorities; 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.

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