BioMarin Receives FDA Approval for VOXZOGO™ (vosoritide) for Injection, Indicated to Increase Linear Growth in Children with Achondroplasia Aged 5 and Up with Open Growth Plates

1st Therapeutic Treatment for Achondroplasia, Most Common Form of Disproportionate Short Stature

Investor Conference Call and Webinar to be Held on Friday, Nov. 19 at 11:30 AM Eastern

SAN RAFAEL, Calif., Nov. 19, 2021 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that the U.S. Food and Drug Administration (FDA) has granted accelerated approval to VOXZOGO™ (vosoritide) for Injection, indicated to increase linear growth in pediatric patients with achondroplasia five years of age and older with open epiphyses (growth plates). This indication is approved under accelerated approval based on an improvement in annualized growth velocity (AGV). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory studies. To fulfill this post-marketing requirement, BioMarin intends to use the ongoing open-label extension studies compared to available natural history.

Voxzogo is the first FDA approved treatment for children with achondroplasia. In patients 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.

"Voxzogo is a medical first that is rooted in BioMarin's focus on molecular genetics and targets the underlying cause of the condition. More than a decade of scientific research underpins the medical advance that Voxzogo represents. We thank the FDA for recognizing its value as the first therapeutic treatment option for children with achondroplasia," said Jean-Jacques Bienaimé, Chairman and Chief Executive Officer of BioMarin. "We extend our gratitude to the community, clinical investigators and the children and their families, who participated and continue to participate in our comprehensive clinical research program as we continue to investigate the full potential of vosoritide."

"Achondroplasia is a lifelong genetic condition resulting from the disordered skeletal architecture caused by impaired endochondral bone growth throughout childhood," said Lynda Polgreen, M.D., an investigator in clinical trials for Voxzogo and an Investigator at The Lundquist Institute at Harbor-UCLA Associate Professor at David Geffen School of Medicine – UCLA. "This approval is an important milestone representing the first time that physicians will be able to offer a therapy targeted at the root cause of the condition for families of children with achondroplasia aged five and older."

"We applaud the FDA for recognizing the urgent unmet medical need for this progressive condition. As a parent of a child with achondroplasia, I see the availability of treatments that impact bone growth as an important step forward," said Amer Haider Co-Founder of Growing Stronger, an organization with a mission to improve the quality of medical care for little people through supporting research. The organization raises nonprofit donations that are granted to researchers focused on dwarfism.

Mr. Haider added, "BioMarin continues to support the achondroplasia community and has a long track record of advancing the standard of care in rare genetic conditions."

With this approval, the FDA also issued a Rare Pediatric Disease Priority Review Voucher (PRV), which confers priority review to a subsequent drug application that would not otherwise qualify for priority review. The rare pediatric disease PRV program is designed to encourage development of new drugs and biologics for the prevention or treatment of rare pediatric diseases.

Voxzogo is expected to be available in the United States by mid- to late-December, and BioMarin will begin the promotion of Voxzogo immediately.

The approval was based on the outcomes of a global randomized, double-blind, placebo-controlled Phase 3 study evaluating the efficacy and safety of Voxzogo and the open-label extension of this Phase 3 study. The study enrolled 121 children aged 5 to 14.9 with achondroplasia. Baseline mean AGV in the placebo and Voxzogo groups was 4.06 cm/year and 4.26 cm/year, respectively. At week 52, the change from baseline in AGV was -0.17 cm/year for the placebo treated patients and 1.40 cm/year for the Voxzogo treated patients, resulting in a statistically significant improvement in AGV of 1.57 cm/year in favor of Voxzogo. After the 52 week double blind, placebo–controlled, phase 3 study, 58 subjects initially randomized to Voxzogo enrolled into an open–label extension. Among the subjects who had two years of follow–up since randomization, the improvement in AGV was maintained.

In August 2021, the European Commission (EC) approved Voxzogo. Marketing authorization reviews are in process in Japan, Brazil, and Australia with potential approvals in these countries in 2022.

Vosoritide Safety

Safety and efficacy of Voxzogo in patients with achondroplasia were assessed in one 52–week, multi–center, randomized, double–blind, placebo–controlled, Phase 3 study. Transient decreases in blood pressure have been observed

with Voxzogo. In the clinical study, 8 (13%) of 60 patients treated with Voxzogo had a total of 11 events of transient decreases in blood pressure compared to 3 (5%) of 61 patients on placebo, over a 52-week treatment period. Patients with significant cardiac or vascular disease or on anti-hypertensive medicine were excluded from the trial. To reduce the risk of a decrease in blood pressure and associated symptoms (dizziness, fatigue and/or nausea), patients should be well hydrated and have adequate food intake prior to administration.

The most common adverse reactions, occurring in greater than or equal to 5% of patients treated with Voxzogo and at a percentage greater than placebo in the Phase 3 study are injection site reactions (including redness, itching, swelling, bruising, rash, hives, pain), vomiting, joint pain, decreased blood pressure, gastroenteritis, diarrhea, dizziness, ear pain, influenza, fatigue, seasonal allergy, and dry skin. See Important Safety Information below and full Prescribing Information and Patient Prescribing Information for additional safety information.

Comprehensive Clinical Development Program

Voxzogo continues to be studied in a broad clinical development program in achondroplasia, and safety and efficacy are being further evaluated across different ages and over time. To date, 243 children with achondroplasia from eight countries have been enrolled in seven BioMarin clinical studies evaluating the safety and efficacy of vosoritide.

Patient Support for Accessing Voxzogo

To reach a BioMarin RareConnections® case manager, please call, toll-free, 1-866-906-6100 or e-mail support@biomarin-rareconnections.com. For more information about Voxzogo, please visit www.voxzogo.com. For additional

information regarding this product, please contact BioMarin Medical Information at medinfo@bmrn.com.

About Achondroplasia

Achondroplasia, the most common form of skeletal dysplasia leading to disproportionate short stature, is characterized by slowing of endochondral bone growth, 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 gain of function mutation 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 change in the gene.

The worldwide incidence rate of achondroplasia is about one in 25,000 live births. Voxzogo is being studied in children whose growth plates are still "open," typically those under 18 years of age. This is approximately 25% of people with achondroplasia. In Latin America, the Middle East, and most of Asia Pacific, there are currently no licensed medicines for achondroplasia.

Investor Conference Call and Webinar to be Held Today at 11:30 AM Eastern Time

Join from a PC, Mac, iPad, iPhone or Android device:

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Zoom Webinar ID: 960 7111 7820

International numbers available here.

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

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for patients with serious and life-threatening rare genetic diseases. The company's portfolio consists of seven commercialized products

and multiple clinical and pre-clinical product candidates. For additional information, please visit www.biomarin.com. Information on such 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. (BioMarin), including, without limitation, statements about: BioMarin's Voxzogo development program generally, the continued approval for this indication may be contingent upon the verification and description of clinical benefit in confirmatory studies and BioMarin's intention to use the ongoing open-label extension studies compared to available natural history to fulfill this post-marketing requirement, the expectation that Voxzogo will be available in the United States by mid- to late-December and BioMarin's intention to begin the promotion of Voxzogo immediately and marketing authorization reviews in process in Japan, Brazil, and Australia with potential approvals in these countries in 2022. 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: final analysis ongoing clinical trials of Voxzogo; our ability to successfully manufacture Voxzogo for the clinical trials and commercially, if approved; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities concerning Voxzogo; and those other risks and uncertainties detailed from time to time under the caption "Risk Factors" and elsewhere in the BioMarin's Securities and Exchange Commission (SEC) filings, including, without limitation, BioMarin's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, and future SEC 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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Contacts:

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

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