U.S. Food and Drug Administration Approves BioMarin's VOXZOGO® (vosoritide) for Children Under 5 Years with Achondroplasia

Oct 20, 2023

Expanded Indication in the U.S. Now Includes Children of all ages with Achondroplasia

SAN RAFAEL, Calif., Oct. 20, 2023 /PRNewswire/ – BioMarin Pharmaceutical Inc. (Nasdaq: BMRN), a global biotechnology company dedicated to transforming lives through genetic discovery, today announced that the U.S. Food and Drug Administration (FDA) has approved the supplemental New Drug Application (sNDA) for VOXZOGO® (vosoritide) to increase linear growth in pediatric patients with achondroplasia with open epiphyses (growth plates). This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Previously, VOXZOGO was indicated for children who were 5 years of age and older. This

expanded indication now includes children of all ages with open growth plates.

"We are pleased that VOXZOGO is now available for children of all ages with achondroplasia," said Hank Fuchs, M.D., president of Worldwide Research and Development at BioMarin. "We are grateful for the collaboration of the achondroplasia community, physicians, and the children and their families who have played a crucial role in advancing this clinical program. We also look forward to further understanding the potential role of VOXZOGO in other genetic short stature conditions, including hypochondroplasia."

"VOXZOGO is the only approved treatment for children with achondroplasia. Until now, it has only been approved in the U.S. for children aged 5 and older with open growth plates," said William Wilcox, M.D., professor of human genetics at Emory University. "I am delighted that VOXZOGO is now approved for younger children where we hope to have potentially greater impact by starting treatment earlier and, as a result, a much longer treatment window."

BioMarin conducted a randomized, double-blind, placebo-controlled Phase 2 clinical trial evaluating the safety and efficacy of VOXZOGO in children aged 5 and under (Study 111-206). Based on the results of this trial, together with evidence from the adequate and well controlled Phase 3 study in pediatric patients aged 5 years and older (Study 111-301), safety and effectiveness of VOXZOGO have been established in pediatric patients of all ages for the improvement in linear growth in children with achondroplasia with open epiphyses. The overall safety profile of VOXZOGO in children under 5 years of age was similar to that seen in older children.

Data from an open-label, long-term Phase 2 extension study was recently presented at the 2023 European Society for Paediatric Endocrinology Meeting in September. Over a four-year period, children aged 2 years and above who received VOXZOGO exhibited a mean (average) height Z-score improvement of 1.1 to 1.4 standard deviations (95% CI limits from 0.46 to 1.93) and a mean height gain of 6.3 to 7.8 centimeters (cm) (95% CI limits from 2.98 to 10.40 cm) when compared to untreated children with achondroplasia of the same age and sex. In addition, children under the age of 2 years, treated with VOXZOGO for three years, had a mean height Z-score improvement of 0.8 to 1.0 standard deviations (95% CI limits from 0.37 to 1.59) and a height gain between 3.5 and 3.9 cm (95% CI limits from 1.57 to 6.16 cm).

Since the introduction of VOXZOGO in 2021, the company has seen strong patient demand for the medicine worldwide. BioMarin has recently been able to secure increased fill-finish commitments in 2024 and beyond to meet this additional demand. There are approximately 800 children under 5 with achondroplasia in the U.S.

VOXZOGO is currently approved in Europe in children with achondroplasia who are 2 years of age and older with open growth plates. In September, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending marketing authorization to expand the indication for VOXZOGO for injection to treat children with achondroplasia aged 4 months and older whose epiphyses are not closed. A final approval decision, typically consistent with the CHMP recommendation, is expected from the European Commission later this year.

VOXZOGO is also approved in Japan in children from birth who have achondroplasia with open growth plates. In addition, it is approved in Brazil in children who are 6 months and older with open growth plates as well as in Australia in children with achondroplasia who are 2 years of age and older with open growth plates.

Orphan Drug Designation in Hypochondroplasia

VOXZOGO also recently received orphan drug designation from the FDA for the treatment of hypochondroplasia, a genetic condition caused by a mutation in the fibroblast growth factor receptor 3 (FGFR3) gene and characterized by impaired bone growth. While similar to achondroplasia, people with hypochondroplasia typically present with milder disproportionality and less severe short stature compared to achondroplasia.

BioMarin plans to initiate a pivotal development program in hypochondroplasia later this year.

About VOXZOGO (vosoritide) for Injection

In children 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 FGFR3. VOXZOGO, a C-type natriuretic peptide (CNP) analog, acts as a positive regulator of the signaling pathway downstream of FGFR3 to promote endochondral bone growth.

VOXZOGO is approved in the U.S. and indicated to increase linear growth in children with achondroplasia with open epiphyses. This indication 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 trial(s). To fulfill this post-marketing requirement, BioMarin intends to use the ongoing open-label extension studies compared to available natural history.

Patient Support Accessing VOXZOGO

To reach a BioMarin RareConnections® Case Manager, please call, toll-free, 1-833-VOXZOGO (1-833-869-9646) or e-mail VOXZOGOSupport@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 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 FGFR3 gene, 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.

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 and open growth plates (epiphyses).
- 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), high levels of blood alkaline phosphatase shown in blood tests, 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 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 and role of VOXZOGO in children with achondroplasia, including younger children, as well as in the treatment of hypochondroplasia and other genetic short stature conditions; the development of BioMarin's VOXZOGO program, including 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; BioMarin's plans for the continued clinical development of VOXZOGO, including ability to maintain continued approval in the U.S. based on ongoing label-extension studies and confirmatory trials; BioMarin's plans to initiate a pivotal development program in hypochondroplasia; and BioMarin's expectations regarding the number of children with achondroplasia that could be prescribed with VOXZOGO and related potential benefits. 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 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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