European Medicines Agency Validates Application for Extension of Indication for VOXZOGO® (vosoritide) for injection to Treat Children with Achondroplasia Under the Age of 2

BioMarin Submits Supplemental New Drug Application to U.S. Food and Drug Administration to Expand Label to Treat Children with Achondroplasia Under the Age of 5

Submissions Based on Favorable Results from Global Randomized Phase 2 Study in Infants and Young Children Demonstrating Increase of Growth Velocity in All Cohorts by Age

Potential to Benefit More than 1,000 Eligible Children in U.S. and Europe

Action by Health Authorities Expected in 2H 2023

SAN RAFAEL, Calif., Jan. 3, 2023 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN), a global biotechnology company dedicated to transforming lives through genetic discovery, announced today that the European Medicines Agency (EMA) validated its Type II Variation application to extend the indication for VOXZOGO® (vosoritide) for injection to treat children with achondroplasia under the age of 2. Validation confirms the submission is complete and begins the EMA's review process. The Company also announced that it submitted a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) to treat children with achondroplasia under the age of 5. Approval of the submissions would mean VOXZOGO could potentially be prescribed as early as birth with more than 1,000 additional children eligible for treatment for achondroplasia, the most common form of disproportionate short stature in humans. The Company anticipates action by health authorities in the second half of 2023.

BioMarin Submits Supplemental Applications for VOXZOGO Indication Extensions for Younger Children; EU Validates

The supplemental marketing applications are based on the outcomes from a Phase 2 randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of VOXZOGO™ (vosoritide) for injection in infants and children aged 3 months to less than five years old.

"We are pleased by results showing an increase in growth velocity across all age cohorts. These data are very encouraging and supportive of expanding the indication to younger children," said Hank Fuchs, M.D., President, Worldwide Research and Development at

BioMarin. "We look forward to further dialogue with health authorities in the U.S. and Europe to review these submissions to expand access to VOXZOGO treatment for this younger age group. Our hope is that children around the world will have the same access as children in Japan where VOXZOGO is approved in all children with achondroplasia, whose growth plates are not closed."

VOXZOGO is the first FDA and EMA approved treatment for children with achondroplasia with open epiphyses (bone growth plates). 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 modified C-type natriuretic peptide (CNP), directly targets the underlying pathophysiology of achondroplasia by down regulating fibroblast growth factor receptor 3 (FGFR3) signaling and consequently promoting endochondral bone formation.

VOXZOGO Safety

The safety profile was generally consistent with that seen in older subjects in the Phase 3 VOXZOGO 301 study (the current label population in the U.S.). Serious Adverse Events (SAEs) were higher in the placebo group (18%) compared to VOXZOGO -treated children (7%). All SAEs, including a fatal respiratory arrest (reported as a sudden infant death syndrome in a treated infant with pre-existing respiratory morbidity), were deemed by the investigators to be unrelated to treatment. 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].

Study Description

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 consists of three cohorts by age (24 months to less than 5 years, 6 months to less than 24 months, less than 6 months) and is followed by a subsequent open-label extension trial where all children receive active treatment. Children in this study have completed a minimum three- or six-month baseline study to determine their respective baseline growth prior to entering the Phase 2 study. The objectives of the study are 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 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 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, 250 children with achondroplasia from eight countries have been enrolled in seven BioMarin clinical studies evaluating the safety and efficacy of VOXZOGO.

VOXZOGO is approved in the U.S. and 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). To fulfill this post-marketing requirement, BioMarin intends to use the ongoing open-label extension studies compared to available natural history.

VOXZOGO is also approved in the E.U., Brazil, and Australia in children with achondroplasia who are 2 years of age and older with open growth plates. It is also approved in Japan in children with achondroplasia who are 0 and older with open growth plates.

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.

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 Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including, without limitation, statements about: BioMarin's vosoritide development program generally and specifically about the Company's submissions of an sNDA to the FDA and a type II variation application to the EMA to treat younger children and the potential for VOXZOGO to indicated for younger children, potentially as early as birth, the timing of action by health authorities, and the benefit of VOXZOGO in younger children. 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 of the Phase 2 study in infants and toddlers, results and timing of current and planned preclinical studies and clinical trials of vosoritide; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities concerning vosoritide particularly as related to the submissions to expand the indicated age range; 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, 2022, 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.

Contacts:
Investors/Media
Traci McCarty
BioMarin Pharmaceutical Inc.
(415) 455-7558

SOURCE BioMarin Pharmaceutical Inc.

---

https://investors.biomarin.com/2023-01-03-European-Medicines-Agency-Validates-Application-for-Extension-of-Indication-for-VOXZOGO-R-vosoritide-for-injection-to-Treat-Children-with-Achondroplasia-Under-the-Age-of-2