BioMarin Receives Positive CHMP Opinion in Europe for Vosoritide for the Treatment of Children with Achondroplasia from Age 2 Until Growth Plates Close

European Commission Decision expected Q3 2021

Temporary Authorization for Use (ATU) Granted in France to Allow Access and Reimbursement of Vosoritide to Begin Immediately

Vosoritide is Potentially the First Medicine to be Approved to Treat Children with Achondroplasia in Europe

Estimated Over 11,000 Children Across Europe, Middle East, and Africa Affected by Achondroplasia and Eligible for Treatment if Approved

FDA Review of Vosoritide NDA Ongoing, PDUFA Target Action Date Nov. 20, 2021

SAN RAFAEL, Calif., June 25, 2021 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced today that the Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending marketing authorization for vosoritide, a once daily injection analog of C-type Natriuretic Peptide (CNP) to treat achondroplasia in children from the age of 2 until growth plates are closed, which occurs after puberty when children reach final adult height. Achondroplasia is the most common form of disproportionate short stature in humans. A final approval decision, typically consistent with the CHMP recommendation, is expected from the European Commission in Q3 2021. Vosoritide is potentially the first medicine to be approved to treat children with achondroplasia in Europe and would be marketed under the brand name VOXZOGO™ (vosoritide).

It is estimated that over 11,000 children across Europe, Middle East, and Africa are affected by achondroplasia and eligible for treatment with vosoritide, if approved by a health authority. Approximately a third of this population are in countries authorized to sell under the EMA license. BioMarin anticipates additional patient access through named patient sales based on an EMA approval in countries in the Middle East and Africa and expects additional market registrations to be facilitated by an anticipated EMA license.

Also, the French National Agency for Medicines and Health Products Safety (ANSM) granted an Autorisation Temporaire d'Utilisation de cohorte (ATU cohort), or Temporary

Authorization for Use to allow access and reimbursement of vosoritide to begin immediately under an authorized process. An ATU allows access to drugs not yet approved in France, when provided for rare diseases, with no alternative options, and when the benefit/risk is presumed positive.

"The positive opinion from the CHMP represents a significant step towards making vosoritide available as a treatment choice for families. The CHMP opinion reinforces the strength of the data and the clinical benefit to children as young as two years old. The temporary authorization granted by the French health authority is a response to the urgency to treat these children," said Hank Fuchs, M.D., President Worldwide Research and Development at BioMarin. "We are committed to the scientifically robust, and rigorous study of vosoritide to continue to demonstrate the safety and efficacy of this investigational therapy that addresses the root cause of achondroplasia. We are committed to providing information to treating physicians and families to determine if a treatment choice is right for them. We are grateful to the patient advocacy groups, our clinical investigators and the children and their families for their participation in this clinical program."

"This positive CHMP opinion represents a significant step toward delivering on the promise of the first pharmacological treatment option for children and families affected by achondroplasia. As a treating physician, I see an urgent demand from families for a treatment option that addresses bone growth," said Klaus Mohnike, Professor of Paediatrics at Magdeburg University Hospital in Germany and investigator for the vosoritide clinical program. "The depth and breadth of the data that supports this opinion builds upon a strong scientific foundation that will continue to increase our understanding of the potential impact of vosoritide on the medical complications that may result from achondroplasia."

"Currently, there is a significant unmet need in achondroplasia. Further research is needed to address serious health complications beyond disproportionate short stature. People with achondroplasia can experience foramen magnum compression, sleep apnea, and spinal stenosis," said Carmen Alonso Alvarez, Managing Director of Fundacion ALPE Foundation. "We commend everyone involved in this effort to bring the potential first medicine to treat children with achondroplasia, which offers the possibility to expand treatment options beyond surgical intervention, address an unmet medical need, and advance the standard of care for our community."

The CHMP based its opinion on the totality of data from the vosoritide clinical development program including the outcomes from the randomized, double-blind,

placebo-controlled Phase 3 study evaluating the efficacy and safety of vosoritide. The Phase 3 Study was further supported by the ongoing long-term safety and efficacy from the Phase 2 dose-finding study, which showed that growth rates have been sustained above participants' baseline rates and above the expected annualized growth velocity for untreated children with achondroplasia throughout the five year observation period for which data are currently available. No acceleration of bone age was observed, suggesting that vosoritide is not reducing the total duration of the growth period. The data package included results from an ongoing Phase 2 randomized double-blind study in infants and young children, including extensive pharmacokinetic and biomarker data, as well as preliminary growth data from participants in the 2 to 5 year age cohort. Data in sentinel study participants showed a positive effect on growth following two years of vosoritide treatment in subjects aged 2 to 5 years. In addition, the data package included the Phase 3 extension study and extensive natural history data.

The CHMP is a scientific committee composed of representatives from the 27-member states of the EU, and Iceland, Norway and Liechtenstein. The committee reviews medical product applications on their scientific and clinical merit and provides advice to the European Commission (EC), which has the authority to approve medicines for the EU.

Vosoritide Safety

Vosoritide, administered in approximately 38,000 injections, was generally well tolerated at all doses. The majority of adverse events (AEs) were mild and no serious adverse events (SAEs) were reported as study drug related. Across all doses, injection site reactions and hypotension were the most common drug-related AEs. All injection site reaction events were transient. AEs of hypotension were mild and transient with majority being asymptomatic and reported in the context of routine blood pressure measurements with minimal clinical impact. No new safety findings were observed. There were no AEs related to disproportionate bone growth or bone pathology. There has been no evidence of accelerated bone age (as assessed by radiologists blinded to the age of the subjects) or negative changes in bone mineral density.

Regulatory Status

The U.S. New Drug Application (NDA) for vosoritide is under review by the FDA with a Prescription Drug User Fee Act (PDUFA) target action date of November 20, 2021. The Company successfully closed out the in-person FDA pre-approval inspection of its manufacturing facilities for vosoritide earlier this year.

In January 2021, the Company received notice from the FDA that the NDA for vosoritide had been granted Priority Review Designation based on the serious pediatric indication it addresses, and the lack of treatment options currently available. Consistent with FDA's policy on changes to review classification for an ongoing application review, the PDUFA action date is not affected by this designation. If approved, the vosoritide NDA may qualify for a Priority Review Voucher (PRV). A PRV confers priority review to a subsequent drug application that would not otherwise qualify for that designation. The rare pediatric disease review voucher program is designed to encourage development of new drugs and biologics for the prevention or treatment of rare pediatric diseases.

Vosoritide received orphan drug designation from the FDA and EMA for the treatment of children with achondroplasia. The Orphan Drug Designation program is intended to advance the evaluation and development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions.

Description of Phase 3 Study and Extension

The global Phase 3 study was a randomized, double-blind, placebo-controlled study of vosoritide in 121 children with achondroplasia aged 5 to 14 for 52 weeks. (The enrollment age criteria are 5 to 18 per the study protocol). Vosoritide is being tested in children whose growth plates are still open. This is approximately 25% of people with achondroplasia. Children in this study completed a minimum six-month baseline study to determine their respective baseline growth velocity prior to entering the Phase 3 study. The primary endpoint of the study is the change in growth velocity from baseline over one year in children treated with vosoritide compared to placebo. A wide range of secondary and exploratory endpoints include anthropometric measures such as height Z-score, body and limb proportionality and joint geometry; biochemical, biomarker and radiological assessments of bone growth and health; and evaluations of health-related quality of life (HRQoL), developmental status, and functional independence. These additional endpoints address the overall impact vosoritide has on achondroplasia and will continue to be evaluated in an ongoing open-label extension study where all subjects receive active treatment.

The ongoing open-label long-term extension study to the completed pivotal, double-blind, placebo-controlled study of vosoritide in children with achondroplasia has a total of 119 children enrolled in the extension study after completion of the pre-treatment observation period and one year of treatment in the pivotal phase 3 study, and all are receiving open-label treatment with vosoritide 15 mcg/kg daily.

Description of Phase 2 Dose Finding Study

The primary objectives of the open-label, sequential cohort, dose-finding study were to evaluate the safety and tolerability of daily subcutaneous vosoritide and to determine the dose to carry forward to Phase 3. Secondary objectives were to evaluate the effects of vosoritide on change from pre-treatment baseline in annualized growth velocity (cm/year), height Z-scores, and body segment proportionality, the vosoritide pharmacokinetic (PK) profile, and biomarkers of vosoritide activity, and endochondral ossification. The study is followed by the ongoing open label extension study to evaluate long-term safety and efficacy of vosoritide.

Description of Phase 2 Study in Infants and Toddlers

The fully enrolled Phase 2 study is an ongoing randomized, placebo-controlled study of vosoritide in approximately 70 infants and young children with achondroplasia ages zero to less than 60 months for 52 weeks. The study is followed by a subsequent open-label extension. Children in this study will have completed a minimum six-month baseline study to determine their respective baseline growth prior to entering the Phase 2 study. The primary objectives of the study are to evaluate safety, tolerability, and the effect of vosoritide on height Z-scores, which is the number of standard deviations in relation to the mean height of age-matched, average stature children. The study also evaluates the PK profile of vosoritide and effects on specific biomarkers of chondrocyte activity. The company also plans to augment the height Z-score data with assessments including proportionality, functionality, quality of life, sleep apnea, and foramen magnum dimension, as well as the advent of major illnesses and surgeries.

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. Beyond disproportionate short stature, people with achondroplasia can experience serious health complications, including foramen magnum compression, sleep apnea, bowed legs, mid-face hypoplasia, permanent sway of the lower back, spinal stenosis and recurrent ear infections. Some of these complications can result in the need for invasive surgeries such as spinal cord decompression and straightening of bowed legs. In addition, studies show increased mortality at every age.

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. Vosoritide is being tested in children whose growth plates are still "open", typically those under 18 years of age. This is approximately 25% of people with achondroplasia. In the U.S., Europe, Latin America, the Middle East, and most of Asia Pacific, there are currently no licensed medicines for achondroplasia.

About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for patients with serious and life-threatening rare and ultra-rare genetic diseases. The company's portfolio consists of six 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 vosoritide development program generally and specifically about the anticipated final approval decision for vosoritide expected from the European Commission in Q3 2021, access and reimbursement of vosoritide to begin immediately in France, the status of the FDA's review of BioMarin's vosoritide U.S. New Drug Application (NDA) and the anticipated PDUFA Target Action Date of November 20, 2021, BioMarin's anticipation that there will be additional patient access to vosoritide through named patient sales based on an EMA approval in countries in the Middle East and Africa, BioMarin's expectation that additional market registrations will be facilitated by an anticipated EMA license and the potential for the vosoritide NDA to qualify for a Priority Review Voucher.

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 3 data, results and timing of current and planned preclinical studies and clinical trials of vosoritide; our ability to successfully manufacture vosoritide 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 vosoritide; 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 March 31, 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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