Food and Drug Administration Accepts BioMarin's New Drug Application for Vosoritide to Treat Children with Achondroplasia

If approved, 1st Therapy in U.S. for the Treatment of Achondroplasia

PDUFA Action Date is Aug. 20, 2021

SAN RAFAEL, Calif., Nov. 2, 2020 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that the U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) for vosoritide, an investigational, once daily injection analog of C-type Natriuretic Peptide (CNP) for children with achondroplasia, the most common form of disproportionate short stature in humans. This acceptance by the FDA marks the first marketing application accepted for a treatment for achondroplasia in the United States

The Prescription Drug User Fee Act (PDUFA) action date is Aug. 20, 2021. The FDA has informed the company that they are not currently planning to hold an advisory committee meeting to discuss the application.

Although the FDA did not identify any filing issues with the NDA, the Agency reiterated a position raised during the Pediatric Advisory Committee (PAC) and Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) held on May 11, 2018 recommending two-year controlled trials in different age groups. BioMarin believes the highly persuasive outcomes from the one-year randomized, double-blind, placebo-controlled Phase 3 trial, coupled with data from the Phase 2 program with up to 5 years of long-term follow-up that has been compared to robust natural history data on growth, offers a rigorous and reliable method to assess whether vosoritide has a durable impact on the rate of endochondral bone growth that ultimately increases final adult height. This

information was included in the marketing application.

While not part of the vosoritide marketing application, in Q4, the Company is also expecting to complete enrollment in a Phase 2 randomized, placebo-controlled study of vosoritide in approximately 70 infants and young children with achondroplasia, aged zero to less than 60 months, for a period of 52 weeks. The study will be followed by a subsequent open-label extension trial when all subjects receive active treatment. Children in this study will complete a minimum three-month baseline study to determine their respective baseline growth prior to dosing in the Phase 2 study. Children in this study will have completed a minimum three-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 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.

"We are looking forward to working with the FDA and other regulatory authorities to evaluate the safety and efficacy of the potentially first pharmacological treatment for children with achondroplasia. In addition to the completed clinical studies included in the application, we have included a natural history study to understand the progression of achondroplasia and medical implications," said Hank Fuchs, M.D., President Worldwide Research and Development at BioMarin. "Our extensive development program has been focused on addressing the underlying cause of achondroplasia. We continue to respect the community's range of views around treatment options. We are grateful to the families who have participated in the clinical trials, the advocacy groups from around the world, and the study investigators, all who have been on this journey with us to deliver a treatment choice and contribute to further

understanding achondroplasia medically and scientifically."

"This is important progress that could lead to the first pharmacological treatment of the underlying cause of achondroplasia. As a treating physician, I feel that it is very important that such treatment options become available to families who may want to consider them for their child," said John A. Phillips III, M.D., Vanderbilt University Medical Center (David T Karzon Professor of Pediatrics) and investigator for the vosoritide clinical program. "The comprehensive clinical program for vosoritide provides scientific and clinical knowledge that focuses on the safety and efficacy of vosoritide and better understanding of the basic cause of achondroplasia, its natural history and treatment."

"We are hopeful that our community is one step closer to having access to the first therapeutic choice for children and families affected by achondroplasia," said Munira Haider, co-founder of Growing Stronger. "We advocate for rigorous scientific and medical research to improve the quality of medical care for little people."

Growing Stronger's mission is to improve the quality of medical care for people through supporting research. The organization raises nonprofit donations that are granted to researchers focused on dwarfism.

Regulatory Status in the U.S. and Europe

BioMarin previously announced that the European Medicines Agency (EMA) validated the Company's Marketing Authorization Application. Vosoritide has also 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.

About Achondroplasia

Achondroplasia, the most common form of 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 mutation 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 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 BioMarin's website is not incorporated by reference into this press release.

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, the possibility of regulatory approval of vosoritide, the FDA's PDUFA action date and the timing of regulatory review, and expectations regarding an advisory committee meeting. 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: our ability to successfully manufacture vosoritide; 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 June 30, 2020, 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

Debra Charlesworth
BioMarin Pharmaceutical Inc.
(415) 455-7451

SOURCE BioMarin Pharmaceutical Inc.
