BioMarin Announces Positive Final Results from Placebo-Controlled Phase 3 Data in Children with Achondroplasia Treated with Vosoritide

Placebo-adjusted Increase in Growth Velocity of 1.6 cm/yr (p<0.0001) in Children Treated with Vosoritide Over One Year
Pre-submission Meetings with Health Authorities Planned for H1 2020 to Discuss Marketing Applications

SAN RAFAEL, Calif., Dec. 16, 2019 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today reported positive final results from its randomized, double-blind, placebo-controlled Phase 3 study evaluating the efficacy and safety of vosoritide. The placebo-adjusted change from baseline in growth velocity after one year of treatment with vosoritide, the primary endpoint, was 1.6 cm/yr (p<0.0001). Vosoritide is an investigational, once daily injection analog of C-type Natriuretic Peptide (CNP). The study enrolled 121 children aged 5 to 14 with achondroplasia, the most common form of disproportionate short stature. The results were consistent across the broad patient population studied. Vosoritide was generally well tolerated with no clinically significant blood pressure decreases. Based on these results, the Company plans to meet with health authorities in the first half of 2020 to discuss plans for submitting marketing applications.

"This is an important milestone that further reinforces our confidence in the tremendous potential of vosoritide. The placebo-controlled study demonstrated a strong increase in growth velocity across the broad population studied," said Hank Fuchs, M.D., President Worldwide Research and Development at BioMarin. "These results when combined with the long-term benefits seen in the Phase 2 study provide hope for a significant and sustained benefit for children with achondroplasia. We appreciate the children and their families who have participated in this development program, and we look forward to discussing plans for submitting marketing applications with health authorities. We also plan to present the detailed data from this study at an upcoming medical meeting."

"As a treating physician, it is exciting to see these compelling results of an investigational therapy confirming its potential to be the first medical therapy to treat the underlying cause of achondroplasia," said John A. Phillips, III, M.D., Vanderbilt University Medical Center (David T Karzon Professor of Pediatrics). "Importantly, this data adds to an increasing body of scientific data on a potential breakthrough in the treatment for achondroplasia."

"Growing Stronger supports medical research that has the potential to improve the quality of medical care and make a significant impact on the lives of little people," said Amer Haider, Founder and President of Growing Stronger. "We are hopeful that supporting research and continuing advances in science will accelerate the development of therapeutic choices for families, where there are no medicines available today."

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.

Description of Phase 3 Study

The global Phase 3 study is 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 is 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 have 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.

Vosoritide Safety

Vosoritide, administered at 15ug/kg/day in this Phase 3 randomized, double-blinded placebo-controlled study over one year, was generally well tolerated. The majority of adverse events (AEs) were mild and no serious adverse events were reported as study drug-related. Injection site reactions were the most common drug-related AEs, and all were transient. No clinically significant blood pressure decreases or new safety findings were observed.

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 and the Middle East, 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 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 Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including, without limitation, statements about: the development of BioMarin's vosoritide development program generally and specifically about the results of the Phase 3 trial, the continued clinical development of vosoritide and the timing and conduct of such clinical program; the possible results of such studies, and discussions with health authorities about marketing applications. 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 enroll participants into such clinical trials, 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 September 30, 2019, 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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