BioMarin Announces Oral Presentation at ENDO2021, the Endocrine Society's Annual Meeting, with Data Demonstrating 2 Years of Treatment Benefit in Children with Achondroplasia Treated with Vosoritide

Height Gain is Maintained in 2nd Year of Treatment

SAN RAFAEL, Calif., March 20, 2021 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that data from the open-label long-term extension of the Phase 3 study of 15 µg/kg dose of vosoritide was presented at an oral presentation at ENDO21, the Endocrine Society's Annual Meeting by Professor Ravi Savarirayan, M.B., B.S., M.D., clinical investigator from the Murdoch Children's Research Institute, Royal Children's Hospital, University of Melbourne, Parkville, Victoria. Vosoritide is an investigational, once daily injection analog of C-type Natriuretic Peptide (CNP) for the treatment of achondroplasia, the most common form of disproportionate short stature in humans.

The data from the open-label extension presented at ENDO21 showed that children maintained an increase in Annual Growth Velocity (AGV) through the second year of continuous treatment with vosoritide. Children who received two years of vosoritide therapy had a baseline mean AGV of 4.28 cm/year. After one year of treatment, mean AGV was 5.71 cm/year and after the second year mean AGV was 5.65 cm/year, demonstrating sustained restoration of a major portion of the growth deficit in achondroplasia through the second year of treatment. Children also had an improved height z-score, which is a measure of height relative to that of a similar population of average height.

In the children who were crossed over from placebo to vosoritide in the open-label extension arm, similar efficacy after one year was observed compared to children who received treatment with vosoritide after one year. Children who

were crossed over to treatment had a baseline mean AGV of 3.99 cm/year. After one year of treatment, mean AGV was 5.57 cm per year.

Retention of subjects on treatment was high with 93% of patients originally randomized to receive vosoritide remaining on treatment two years later.

"This is an important extension of the original study's findings and confirm that the benefits of vosoritide are sustained during treatment through two years," said Savarirayan. "While these two-year data are encouraging at showing a durable treatment effect, longer term follow-up will provide additional insights on improvements in body proportions and whether such improvements can potentially make a difference in certain aspects of a child's life."

"Maintaining a consistent level of growth is important because it supports that vosoritide is addressing the root cause of achondroplasia," said Melita Irving, Clinical Geneticist at Guy's and St Thomas' NHS Foundation Trust, London, UK and investigator for the vosoritide clinical program at the Evelina London Children's Hospital. "The clinical program for vosoritide is robust and will continue to evaluate the impact on other important medical outcomes in achondroplasia through long-term evaluation. Overall, the data are encouraging, and allows us to imagine the potential for this first and only targeted precision treatment for achondroplasia."

"We continue to take a relentless approach to advance our understanding of how vosoritide could potentially benefit children with achondroplasia, and to collect the information families and physicians will need to make informed decisions about the choice of treatment," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "We are encouraged by the consistency of this data with our expectations based on the known biology of CNP effects on growth, and with earlier studies, specifically with regards to durability of effect in absence of pathological advancement of bone age. We

are grateful to the children, families and investigators for participating in this study and allowing the opportunity for the scientific exchange of clinical data at medical meetings like ENDO2021."

Vosoritide Safety

The 2-year data demonstrated that vosoritide, administered at 15ug/kg/day was generally well tolerated with no new safety findings. 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. There were no AEs related to disproportionate bone growth or bone pathology. No clinically significant blood pressure decreases or new safety findings were observed.

Regulatory Status

In 2020, the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) accepted and validated the marketing authorization application for vosoritide for achondroplasia. The Committee for Medicinal Products for Human Use (CHMP) opinion is expected in Europe in June of 2021. 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 August 20, 2021. In the United States, the Company has chosen to provide the 2-year outcomes from the Phase 3 extension study to the FDA as additional data to convey the vosoritide treatment effect and long-term durability. The Company believes that supplying this additional data could result in a major amendment, resetting the current PDUFA target action date out three months to November.

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.

Upon the acceptance of the regulatory submission for vosoritide, 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 and the updated 2-year data from the Phase 3 study, 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.

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.

Description of Phase 3 Extension Study

This is an ongoing open-label long-term extension study to a completed pivotal, double-blind, placebo-controlled study of vosoritide in children with achondroplasia. A total of 119 children were 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. Vosoritide is being tested in children whose growth plates are still "open." This is approximately 25% of people with achondroplasia. The extension study is evaluating safety, AGV, and cumulative annual height gain until participants reach final adult height. 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.

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 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 extension of the Phase 3 trial, the timing of actions by regulatory authorities including the expectation of the CHMP opinion for vosoritide in Europe in June of 2021; the potential for the vosoritide NDA, if approved, to qualify for a Priority Review Voucher; and the plan to submit the second year of Phase 3 data to the FDA and the potential that this could result in a major amendment, resetting the

current PDUFA date out three months to November. 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 extension 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 record data during a global pandemic, 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 Annual Report on Form 10-K for the year ended December 31, 2020, as such factors may be updated by any subsequent reports. 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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