BMN 111 (vosoritide) Improves Growth Velocity in Children With Achondroplasia in Phase 2 Study

50% Increase in mean annualized growth velocity in 15 µg/kg/daily dose group

BMN 111 was well tolerated across all three dose cohorts

Phase 2 findings support program advancement of 15µg/kg/daily dose into pivotal registration discussions with health authorities

Investor conference call to be held today, June 17, 2015 at 1:30pm PT/(4:30pm ET)

SAN RAFAEL, Calif., June 17, 2015 (GLOBE NEWSWIRE) -- BioMarin Pharmaceutical Inc. (Nasdaq:BMRN) today announced positive results of a Phase 2 proof-of-concept and dose finding study of BMN 111 (vosoritide), an analog of C-type Natriuretic Peptide (CNP), in children with achondroplasia. Achondroplasia is the most common form of human dwarfism. Vosoritide has Orphan designation in both the United States and Europe.

Phase 2 Results and Safety Summary of First Six Months

Data from the 26 children participating in the Phase 2 study demonstrated a favorable safety profile and efficacy at the 15 micrograms/kilogram/daily dose. The 10 children in Cohort 3 treated with 15 micrograms per kilogram per day had a mean increase of 50% (p-value = 0.01) in their annualized growth velocity compared to their annualized prior 6 month natural history baseline growth velocity. Changes from baseline in proportionality as measured by upper to lower body ratio were not observed. No Serious Adverse Events (SAEs) were observed for the duration of the study. The complete data from the study will be presented at a medical meeting later in the year.

"We are very encouraged to have observed evidence of activity with vosoritide in children participating in our Phase 2 study," said Wolfgang Dummer, M.D., Ph.D., Vice President, Clinical Development of BioMarin. "In children receiving the highest dose of 15 micrograms per kilogram daily, we observed a 50% increase in mean annualized growth velocity compared to their own natural history control growth velocity. This increase in growth velocity, if maintained, could allow children with achondroplasia to resume a normalized growth rate." Dr. Dummer continued, "More importantly, vosoritide was well tolerated in all dose cohorts and we have observed no major safety concerns to date. Based on these results, we intend to move into pivotal registration study discussions with health authorities with a dose of 15 micrograms per kilogram daily. In addition, to support

further exploration of a dose that may enable "catch-up" growth in the event of delayed treatment, we intend to study 30 micrograms per kilogram daily in ancillary studies. The next step in our development plan is to review this Phase 2 data with health authorities and our outside advisors to develop our path forward with registration enabling studies."

"We are looking forward to working with health authorities worldwide as we continue to develop vosoritide for patients with achondroplasia globally," said Jean-Jacques Bienaimé, Chairman and Chief Executive officer at BioMarin. "It is estimated that about 96,000 patients in our established territories are afflicted with achondroplasia, so approximately 25%, or 24,000, are under 18 years of age and in our addressable market."

Safety and Adverse Event Observations in the Phase 2 Study

- No serious adverse events (SAEs) were reported in any cohort during the study.
- The majority of AEs reported were mild (Grade 1) and included injection site reactions, headache, hypotension, back pain and cough.
- Blood pressure (BP) and heart rate (HR) were monitored frequently and during every site visit. Symptomatic hypotension was not documented in the study. Each patient had approximately 100 measurements of BP in the course of the study. 17 asymptomatic hypotension events in 10 patients were recorded out of the majority of blood pressure measurements obtained. The 17 events were mild (Grade 1), transient, self-limited and resolved without medical intervention. Events occurred across all dose cohorts and at varying times after dosing with no evidence of dose dependency. One subject in Cohort 1 was reported to have "dizziness due to hypotension" and the event resolved without medical intervention in 5 minutes. The event occurred at home and no blood pressure measurement available during the episode of dizziness. The patient continued therapy with no further events.
- No clinically significant changes in vital signs at any dose or time of exposure.
- No bone related adverse events (AEs) were reported.

Table 1: BMN 111 (vosoritide) Summary of Efficacy Results from Phase 2 Study in Children with Achondroplasia

Efficacy Analysis: Annualized 6-Months Growth Velocity

	Cohort 1	**Cohort 2**	**Cohort 3**
Growth Velocity	2.5 µg/kg/daily **(n=8*)**	7.5 µg/kg/daily **(n=8)**	15 µg/kg/daily **(n=10)**
Baseline			

Mean (cm/Year)	**3.8**	**2.9**	**4.0**
Post-Treatment			
Mean (cm/year)	**3.4**	**4.2**	**6.1**
Change from Baseline			
Mean (cm/year)	**-0.4**	**1.3**	**2.0**
95% Confidence Interval (cm/year)	**-1.8, 1.1**	**0.1, 2.5**	**0.6, 3.4**
p-value**	**0.56**	**0.04**	**0.01**
Percent increase from Baseline			
Based on means (%)	**NM**	**45**	**50**

* One subject withdrew from study prior to the 6-month visit, all summaries for Cohort 1 were based on 7 subjects.

** p-value, provided for descriptive purposes and based on the paired t-test comparing post-treatment GV and baseline GV, not adjusted for multiple comparisons.

Additional Highlights from BMN 111 (vosoritide) Study in Children with Achondroplasia

- There was a dose-related increase in urinary excretion of cGMP measured over the 6 month duration of the study. cGMP is a biochemical marker that may indicate that BMN 111's biological effect will continue beyond 6 months.
- In dose cohort 3, the median annualized increase from baseline was 2.7 centimeter/year or 66% annualized increase over baseline.

Phase 2 Study Design

Children in this study completed a minimum six month natural history 901 study to determine their respective baseline growth velocity prior to entering the Phase 2 study with BMN 111. The Phase 2 trial was an open-label, sequential cohort dose-escalation study of BMN 111 in children with achondroplasia. In this three dose cohort study, patients were treated with either 2.5 µg/kg/daily, 7.5 µg/kg/ daily or 15 µg/kg/ daily, respectively. A total of 26 children with achondroplasia with an average age of 7.8 years were enrolled in the study. Based on the safety profile observed to date across the three dose cohorts, all subjects participating in the Phase 2 study have now been switched to the highest dose of 15 µg/kg/ daily for the duration of the 18 month extension study.

BMN 111 was recently designated the generic name *vosoritide* by the International Nonproprietary Names (INN) system managed by the World Health Organization (WHO).

Conference Call Details

BioMarin will host a conference call and webcast to discuss Phase 2 results with BMN 111 on June 17, at 4:30 p.m. ET/1:30 .m. PT. This event can be accessed on the investor section of the BioMarin website at www.BMRN.com.

U.S. / Canada Dial-in Number: 877.303.6313

International Dial-in Number: 631.813.4734

Conference ID: 68336725

Replay Dial-in Number: 855.859.2056

Replay International Dial-in Number: 404.537.3406

Conference ID: 68336725

About Achondroplasia

Achondroplasia is the most common form of human dwarfism and is characterized by failure of normal conversion of cartilage into bone, which results in disproportionate short stature. This condition is caused by a mutation in the fibroblast growth factor receptor 3 gene (FGFR3), a negative regulator of bone growth. Disproportionate growth between endochondral bone and underlying organs leads to a number of orthopedic, neurological, respiratory, ear, nose, and throat (ENT) issues and increased mortality. 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, recurrent ear infections and obesity. Some of these complications can result in invasive surgeries such as spinal cord decompression and straightening of bowed legs. Some people with achondroplasia suffer from chronic pain and regularly confront a world not built for them. Currently there is no FDA-approved treatment for achondroplasia. BMN 111 is being studied in children with achondroplasia under the age of 18 because their bones are still amenable to 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, per the World FactBook 2014 edition which translates into approximately 96,000 potential patients. The initial opportunity is about 25 percent of the incidence number because vosoritide is being tested in children whose growth plates are still "open," typically those under 18 years of age.

About BioMarin

BioMarin develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions. The company's product portfolio comprises five approved products and multiple clinical and pre-clinical product candidates. Approved products include Vimizim® (elosulfase alfa) for MPS IVA, a product wholly developed and commercialized by BioMarin; Naglazyme® (galsulfase) for MPS VI, a product wholly developed and commercialized by BioMarin; Aldurazyme® (laronidase) for MPS I, a product which BioMarin developed through a 50/50 joint venture with Genzyme Corporation; Kuvan® (sapropterin dihydrochloride) Powder for Oral Solution and Tablets, for phenylketonuria (PKU), developed in partnership with Merck Serono, a division of Merck KGaA of Darmstadt, Germany and Firdapse® (amifampridine), which has been approved by the European Commission for the treatment of Lambert Eaton Myasthenic Syndrome (LEMS). Product candidates include drisapersen, an exon skipping oligonucleotide, for which a marketing application has been submitted to FDA and EMA for the treatment of patients with Duchenne muscular dystrophy (DMD) with mutations in the dystrophin gene that are amenable to treatment with exon 51 skipping, pegvaliase (PEGylated recombinant phenylalanine ammonia lyase, formerly referred to as BMN 165 or PEG PAL), which is currently in Phase 3 clinical development for the treatment of PKU, talazoparib (formerly referred to as BMN 673), a poly ADP-ribose polymerase (PARP) inhibitor, which is currently in Phase 3 clinical development for the treatment of germline BRCA breast cancer, reveglucosidase alfa (formerly referred to as BMN 701), a novel fusion protein of insulin-like growth factor 2 and acid alpha glucosidase (IGF2-GAA), which is currently in Phase 3 clinical development for the treatment of Pompe disease, BMN 111 (vosoritide), a modified C-natriuretic peptide, which is currently in Phase 2 clinical development for the treatment of achondroplasia, BMN 044, BMN 045 and BMN 053, exon skipping oligonucleotides, which are currently in Phase 2 clinical development for the treatment of Duchenne muscular dystrophy (exons 44, 45 and 53), cerliponase alfa (formerly referred to as BMN 190), a recombinant human tripeptidyl peptidase-1 (rhTPP1) for the treatment of CLN2 disorder, a form of Batten disease, which is currently in development, BMN 270, an AAV-factor VIII vector, for the treatment of hemophilia A and BMN 250, a novel fusion of alpha-N-acetyglucosaminidase (NAGLU) with a peptide

derived from insulin-like growth factor 2 (IGF2), for the treatment of MPS IIIB.

For additional information, please visit www.BMRN.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., including, without limitation, statements about: the development of BMN 111 (vosoritide); the continued clinical development of vosoritide; the final results of the Phase 2 trial of vosoritide, and actions by regulatory authorities. 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: results and timing of current and planned preclinical studies and clinical trials of vosoritide; 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 factors detailed in BioMarin's filings with the Securities and Exchange Commission, including, without limitation, the factors contained under the caption "Risk Factors" in BioMarin's 2014 Annual Report on Form 10-K, and the factors contained in BioMarin's reports on Form 10-Q. Stockholders are urged not to place undue reliance on forward-looking statements, which speak only as of the date hereof. BioMarin is under no obligation, and expressly disclaims any obligation to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

CONTACT: Investors:

Traci McCarty

BioMarin Pharmaceutical Inc.

(415) 455-7558

Media:

Debra Charlesworth

BioMarin Pharmaceutical Inc.

(415) 455-7451

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