BioMarin InvestorRoom

BioMarin Highlights Breadth of Innovative Development Pipeline at R&D Day on October 18th in New York

Selection of BMN 290 Next IND Drug Development Candidate for Treatment of Friedreich's Ataxia
BMN 270 gene therapy for Severe Hemophilia A: IND and CTA Active, Phase 3 to start 4Q17
Vosoritide for Achondroplasia Demonstrates Sustained Increase in Annualized Growth Velocity Over 30 Months of Treatment
Pegvaliase BLA on Track for FDA Action 1H 2018, EU MAA Filing Q1 2018

SAN RAFAEL, Calif., Oct. 18, 2017 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) updated the investment community on the Company's development portfolio, which is focused on innovative therapies to treat rare and ultra-rare diseases.

"We are pleased to share the progress of our development programs in therapies to treat rare genetic diseases; hemophilia A, PKU, achondroplasia and our next IND into Friedreich's Ataxia," said Hank Fuchs, M.D., President Worldwide Research and Development of BioMarin. "In the near term, we are expecting an FDA decision on pegvaliase to treat adults with uncontrolled PKU in the first half of next year, and we continue to be rapidly and decisively developing the potential first gene therapy for severe hemophilia A."

BioMarin Selects BMN 290 for Friedreich's Ataxia

BioMarin announced today that it has selected BMN 290, a selective chromatin modulation therapy, for the treatment of Friedreich's Ataxia (FA). FA is a rare autosomal recessive disorder with worldwide prevalence of approximately 15,000, which results in disabling neurologic and cardiac progressive decline. Currently there are no approved disease modifying therapies for FA. In preclinical models, BMN 290 increases frataxin expression in affected tissues more than two-fold. BMN 290 is a second generation compound derived from a compound acquired from Repligen that had human clinical data demonstrating increases in frataxin in FA patients. BMN 290 was selected for its favorable penetration into the central nervous system and cardiac target tissues, and its preservation of the selectivity of the original Repligen compound. The company expects to submit the IND in 2H 2018.

BMN 270 Gene Therapy for Severe Hemophilia A

BioMarin announced today that the FDA has completed their review of the IND application for BMN 270, an investigational gene therapy treatment for severe hemophilia A, and concluded that it can proceed. The IND application included 52-week data at the 6e13 vg/kg dose and the protocol for the Phase 3 study using the 6e13 vg/kg dose. The protocol for the second Phase 3 study using the 4e13 vg/kg dose has also been submitted to the FDA.

BioMarin also announced today that the Phase 3 Clinical Trial Application was approved by the UK Medicines and Healthcare Products Regulatory Agency (MHRA).

The company expects to initiate the global Phase 3 program in the fourth quarter of 2017.

Data Update on Phase 1/2 Study of 4e13 vg/kg Dose

In addition, the company provided an update on the ongoing open-label Phase 1/2 study of the 4e13 vg/kg dose at up to 36 weeks of observation at the September 14, 2017 data cut. Since the last data update provided during the Q2 earnings call on August 2, 2017, five of the six patients at the 4e13 vg/kg dose tracked to the low range of normal, and the sixth is in the mild range for Factor VIII levels. Median annualized bleed and factor VIII use rates for 4e13 and 6e13 vg/kg were zero after Week 4.

Factor VIII Levels (%) of 4e13 vg/kg Dose Patients* by Visit (N=6)

Week**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**
4e13 vg/kg Dose									
n	6	6	6	6	6	6	6	3	3
Median Factor VIII Level*** (%)	4	**15**	**21**	**29**	**34**	**28**	**31**	**51**	**45**

Mean Factor VIII Level*** (%)	**5**	**13**	**19**	**26**	**31**	**29**	**30**	**51**	**47**
Range (low, high)	(2,10)	(3,21)	(6,32)	(5,38)	(7,45)	(7,43)	(4,44)	(48,54)	(41,55)

**All patients had severe hemophilia A, defined as less than or equal to 1% of Factor VIII activity levels, expressed as a percentage of normal factor activity in blood.*

***Weeks were windowed by +/- 2 weeks*

**** Bolded numbers are in the mild to normal range of Factor VIII activity as defined by the World Federation of Hemophilia, http://www.wfh.org/en/page.aspx?pid=643 (link current as of Oct. 17, 2017). Factor VIII levels are determined by one-stage assay.*

BMN 270 Reduces Bleeds and Factor VIII Use: Summary of Mean Annualized Bleeding Rate (ABR) and FVIII Use Rate of 4e13 vg/kg Dose for Patients Previously on Prophylaxis (N=6) at September 14, 2017 data cut

	Before BMN 270 Infusion	**After BMN 270 Infusion**
	Median (mean, SD)	**Median (mean, SD)**
Annualized Bleeding Rate* (bleeding episodes per year per subject)	8.0 (12.2, 15.4)	0.0 (0.8, 1.9)
Annualized FVIII Use Rate* (infusions per year per subject)	155.5 (146.5, 41.6)	0.0 (2.7, 6.7)

**Post-infusion data were based on data after Week 4*

BMN 270 Generic Name is Valoctocogene Roxaparvovec

BioMarin was issued the International Nonproprietary Name (INN) valoctocogene roxaparvovec for BMN 270. The World Health Organization (WHO) has approved the INN "valoctocogene roxaparvovec" for the Company's gene therapy to treat hemophilia A. International Nonproprietary Names (INN) identify pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name.

Gene Therapy Manufacturing

BioMarin has constructed one of the largest gene therapy manufacturing facilities in the world, which is located in Novato, California. Good Manufacturing Practices (GMP) production of BMN 270 has commenced and will support clinical development activities and anticipated commercial demand. This facility is capable of supporting approximately 2,000 patients per year, and the production process was developed in accordance with International Conference on Harmonisation guidance for Pharmaceuticals for Human Use facilitating worldwide registration with health authorities.

Vosoritide Data Update

BioMarin provided an update on its open-label Phase 2 study of vosoritide, an analog of C-type Natriuretic Peptide (CNP), in children with achondroplasia, the most common form of disproportionate short stature in humans.

Vosoritide for achondroplasia demonstrates sustained increase in average growth velocity over 30 months of treatment in 10 children, who completed 30 months of daily dosing at 15 µg/kg/day. Over this period of time, patients have experienced mean absolute growth increase of approximately 4 cm over what their baseline growth velocity would have predicted.

The sustained increase in annualized growth velocity was accompanied by sustained improvements over time in height compared to age- and gender-matched unaffected children as measure by z-scores. In addition, treatment with

vosoritide shows continued improvement over time in proportionality as measured by a ratio of the upper and lower body measurements or U/L ratio.

Pegvaliase Program Update

The Pegvaliase Biologics License Application (BLA) remains on Track for FDA Action during the first half of 2018. The company plans to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in Q1 2018.

2017 Full-year Total Revenue and Non-GAAP Guidance reaffirmed

Today, the Company commented on their Total Product Revenue and Non-GAAP trends for the third quarter and full-year 2017. In terms of the overall commercial business, BioMarin stated that sales of products in markets throughout most of the world are performing at or above internal expectations. However, the Company said the one exception is Brazil, where a slowdown in Federal purchasing orders has extended into the third quarter of this year. As a result, third quarter revenues are expected to be negatively impacted. For the fourth quarter, if orders are placed in Brazil as expected, Total Product Revenue for full-year 2017 is anticipated to be in the mid-point of guidance. However, if sales to Brazil continue to be slow in the fourth quarter, full-year 2017 Total Product Revenue may be at the low end of guidance. Regardless of Brazilian ordering patterns for the remainder of the year, and based on careful expense control, the Company still expects to be in the mid to high-end of Non-GAAP profitability guidance for full-year 2017.

About BioMarin and Disease Information

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 BioMarin's website is not incorporated by reference into this press release.

About Friedreich's Ataxia

Friedreich's ataxia (FA) is a progressive, neurological disorder that affects approximately 15,000 people in the United States and Europe, typically resulting in wheelchair dependence in young adulthood and early death due to cardiac failure. It is caused by mutations in the FXN gene, and is inherited in an autosomal recessive manner. FXN mutations result in reduced expression of frataxin protein, manifesting in progressive neurological and cardiac damage. Major neurological symptoms include muscle weakness and ataxia, a loss of balance and coordination. These symptoms typically appear between 10 and 15 years of age, but FA has been diagnosed in people from ages 2 to 50 with earlier onset associated with a more severe course.

BMN 270 Safety

Overall, BMN 270 has been well-tolerated by patients across all doses, including the two patients that received the lowest doses of 6e12 and 2e13 vg/kg, respectively. No patients developed inhibitors to Factor VIII and no patients withdrew from the study. The most common adverse events (AEs) across all dose cohorts were alanine aminotransferase (ALT) elevation (11 patients, 73%); arthralgia, aspartate aminotransferase elevation, and headache (7 patients each, 47%); back pain and fatigue (5 patients each, 33%). Two patients reported Serious Adverse Events (SAEs) during the study. One patient was hospitalized for observation after developing Grade 2 pyrexia with myalgia and headache within 24 hours of receiving BMN 270. The event resolved within 48 hours following treatment with paracetamol, an over-the-counter treatment for pain and fever. The event was assessed as related to BMN 270. The other SAE was assessed as not related to BMN 270, attributed to a planned knee surgery to treat hemophilic arthropathy, and Grade 1 in severity. No complications were reported.

About Hemophilia A

Hemophilia A, also called Factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective Factor VIII, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation, a new mutation that was not inherited. As an X-linked disorder, hemophilia A mostly affects males, occurring in approximately 1 in 5,000 male births. People living with the disease are not able to form blood clots efficiently and are at risk for excessive bleeding from modest injuries, potentially endangering their life. People with severe hemophilia often bleed spontaneously into their muscles or joints. The standard of care for the 43% of hemophilia A patients who are severely affected, is a prophylactic regimen of Factor VIII infusions three times per week. Even with prophylactic regimens, many patients still experience microbleeds and spontaneous bleeding events that result in progressive joint damage.

Vosoritide Safety

Vosoritide was generally well tolerated at all doses. The majority of adverse events (AEs) were mild and no serious AEs 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, transient and resolved without medical intervention, and the majority were asymptomatic and reported in context of routine blood pressure measurements. No new safety findings were observed at the 30 µg/kg/day dose.

About Achondroplasia

Achondroplasia, the most common form of disproportionate short stature in humans, 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. 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 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 percent of people with achondroplasia. In the United States, Europe, Latin America and the Middle East, there is currently no licensed medicines for achondroplasia.

Pegvaliase Safety

The safety data set for all pegvaliase trials includes exposure up to seven years and approximately 680 patient years of treatment, 300 of which are from the Phase 3 program. Most Adverse Events (AEs) were mild or moderate in severity. 8.5% of patients reported AEs leading to study withdrawal. The most common Adverse Events (AEs) were arthralgia (69.5%), injection site reaction (65.1%), headache (51.9%), nasopharyngitis (41.1%), and rash (40.2%).

Pegvaliase treated patients had acute systemic hypersensitivity adverse events (4.6%) as defined by the broad National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network (NIAID/FAAN) (Sampson's) criteria for anaphylaxis by expert external adjudication. Hypersensitivity adverse events and acute systemic hypersensitivity events mainly occurred in the first year of treatment. With prolonged exposure, AE rates declined for almost all categories. Using high-sensitivity assays, anti-drug IgE was undetected in the observed acute systemic hypersensitivity events. Eight of the 13 patients with acute systemic hypersensitivity events were re-dosed and six of the eight re-dosed patients continued therapy.

About Phenylketonuria

Phenylketonuria (PKU) is a genetic disorder affecting approximately 50,000 diagnosed patients in the developed world and is caused by a deficiency of the enzyme PAH. This enzyme is required for the metabolism of Phe, an essential amino acid found in most protein-containing foods. If the active enzyme is not present in sufficient quantities, Phe accumulates to abnormally high levels in the blood and becomes toxic to the brain, resulting in a variety of complications including severe intellectual disability, seizures, tremors, behavioral problems and psychiatric symptoms. As a result of newborn screening efforts implemented in the 1960s and early 1970s, virtually all individuals with PKU or PAH deficiency under the age of 40 in developed countries are diagnosed at birth and treatment is implemented soon after. PAH deficiency can be managed with a Phe-restricted diet, which is supplemented by low-protein modified foods and Phe-free medical foods; however, the strict diet is difficult for most adult patients to adhere to the extent needed for achieving adequate control of blood Phe levels. To learn more about PKU and PAH deficiency, please visit www.PKU.com. Information on this 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 its development programs and regulatory actions related to these programs, including the expected timing of the filing of the MAA for pegvaliase and an FDA decision on pegvaliase, the timing of its anticipated submission of an IND for BMN 290, BioMarin's BMN 270 program generally, the timing of the initiation of the global Phase 3 program, the expected design and size of the Phase 3 studies and a Phase 1/2 study in subjects with pre-existing antibodies against AAV5, expected regulatory actions related to BMN 270, the expectations of total BioMarin revenues for the third quarter and full year 2017 and the financial performance of BioMarin as a whole, and statements about the anticipated capacity of the Company's gene therapy manufacturing facility. 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 our product candidates, the continued clinical experiences of the patients in the current clinical studies; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities; the content and timing of decisions by local and central ethics committees regarding the clinical trials; our ability to successfully manufacture our product candidates for the preclinical and clinical trials; the ordering patterns for our commercial products, particularly orders from Brazilian governmental entities; and those other risks detailed from time to time under the caption "Risk Factors" and elsewhere in BioMarin's Securities and Exchange Commission (SEC) filings, including BioMarin's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, and future 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	*Debra Charlesworth*
BioMarin Pharmaceutical Inc.	*BioMarin Pharmaceutical Inc.*
(415) 455-7558	*(415) 455-7451*

SOURCE BioMarin Pharmaceutical Inc.
