BioMarin Provides Positive Proof-of-Concept Data for BMN 270 Gene Therapy in Hemophilia A in Late Breaking Oral Presentation at the World Federation of Hemophilia (WFH) 2016 World Congress

6 of 7 High Dose Patients Show Factor VIII levels above 50%, 7th patient above 10%

No Clinically Relevant Sustained Rises in ALT

Phase 2b Study to Begin Mid-2017 for Potential Accelerated Approval Filing

Conference Call and Web-cast with Slides to be Held Wednesday, July 27th at 4:05pm ET

SAN RAFAEL, Calif., July 27, 2016 (GLOBE NEWSWIRE) -- BioMarin Pharmaceutical Inc. (NASDAQ:BMRN) announced today positive interim results of an open-label Phase 1/2 study of BMN 270, an investigational gene therapy treatment for severe hemophilia A at the XXXII International Congress of the World Federation of Hemophilia (WFH). The data was presented in the Late Breaking Gene Therapy session by John Pasi, Professor of Haemostasis and Thrombosis, Barts and the London School of Medicine, Honorary Consultant Haematologist, The Royal London Hospital, and a lead investigator of the study. The data presented at the congress is an update since the Company reported initial results on this same study on April 20, 2016. To access the data presented at the Congress, click here.

A total of nine patients with severe hemophilia A received a single dose of BMN 270, seven of whom have been treated at the highest dose of 6×10^{13} vg/kg. As of the July 6 data cut off, post-treatment follow-up ranges from 12 to 28 weeks. For the seven patients treated with the high dose, as of each patients' most recent reading, six of seven patients had Factor VIII levels above 50%, as a percentage calculated based on the numbers of International Units per deciliter of plasma (IU/dL), and the seventh was above 10%. In addition, four patients who have been followed the longest had a mean Factor VIII level of 146% at their 20 week visit. Two patients with Factor VIII levels above 200% had no unexpected events or need for medical intervention. For the seven patients at the high dose, the median annualized bleeding rate measured from day of gene transfer to data cut of observation period fell to 5 from 20.

No clinically relevant sustained rises in ALT levels or other markers of liver toxicity have been observed. The maximum ALT levels were between 23 and 82 U/L (less than two

times the upper limit of normal, which is 43 U/L for the central laboratory in this study) approximately 12 weeks after gene delivery and generally declined over the next few weeks. ALT rises have not been associated with any decrease in Factor VIII levels. A steroid regimen administered to all high dose patients has been well-tolerated. Patients are successfully tapering off of steroids with two subjects off steroid therapy for up to 2.5 weeks with no adverse impact on Factor VIII expression or ALT levels. Study medication was generally well tolerated. No serious adverse events were observed, and most common adverse events were mild in severity.

"These data provide strong proof of concept evidence that restoration of clotting function may be achieved by gene therapy," said John Pasi, Ph.D. F.R.C.P, Professor of Haemostasis and Thrombosis at Barts and the London School of Medicine and Dentistry and primary investigator for the BMN 270 Phase 1/2 clinical trial. "For the first time, patients have reason to hope to avoid bleeding and the opportunity to live a normal life."

"We look forward to collaborating with experts and health authorities to design the next phase of investigation," said Hank Fuchs, M.D., Chief Medical Officer at BioMarin. "Beginning in mid-2017, a Phase 2b study will seek to evaluate the optimal dose of BMN 270 using Factor VIII expression as the primary endpoint with material from the to-be-commercialized manufacturing process. If successful, this study could support an accelerated approval given the severe unmet need, the substantial effect and tolerability of the treatment."

Phase 1/2 Study Design

The current Phase 1/2 study is evaluating the safety and efficacy of BMN 270 gene therapy in up to 12 patients with severe hemophilia A, as defined by the WFH as less than 1% of blood clotting factor. The primary endpoints are to assess the safety of a single intravenous administration of a recombinant AAV vector coding for human-coagulation factor VIII and to determine the change from baseline of factor VIII expression level at 16 weeks after infusion. The kinetics, duration and magnitude of AAV-mediated factor VIII activity in individuals with hemophilia A will be determined and correlated to an appropriate BMN 270 dose.

This is a dose escalation study with the goal of observing an increase in factor VIII levels. Secondary endpoints include assessing the impact of BMN 270 on the frequency of factor VIII replacement therapy, the number of bleeding episodes requiring treatment and any potential immune responses. Patients will be monitored for safety and durability of effect for five years.

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.[1] As an X-linked disorder, hemophilia A mostly affects males, occurring in approximately 1 in 5,000 male births.[2] 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.[3] Even with prophylactic regimens, many patients still experience microbleeds and spontaneous bleeding events that result in progressive joint damage.

About Gene Therapy

Gene therapy is a treatment designed to alter a genetic problem by adding a corrected copy of the defective gene. The functional gene is inserted into a vector — containing a DNA sequence coding for a specific protein — that acts as a delivery mechanism, providing the ability to deliver the functional gene to cells. The cells can then use the information to build the functional protein that the body needs, potentially reducing or eliminating the cause of the disease. Currently, gene therapy for the treatment of hemophilia A is available only as part of a clinical trial. The AAV approach to gene therapy has been advanced at the University College London (UCL) in the treatment of Hemophilia B. At UCL, this technology has shown evidence to be both safe and effective, correcting bleeding for greater than four years in a continuing clinical trial.

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Interested parties may access a live webcast and slide presentation that will accompany the conference call by going here or accessing the investor section of the BioMarin website, www.biomarin.com. A slide presentation will accompany the conference call and can be seen using the webcast link. Separately, the Late Breaker slide presentation will be available to download in advance of the call. A replay of the call will be archived on the site for one week following the call.

U.S. / Canada Dial-in Number: (866) 502-9859

International Dial-in Number: (574) 990-1362
Conference ID: 52603053

Replay Dial-in Number: (855) 859-2056
Replay International Dial-in Number: (404) 537-3406
Conference ID: 52603053

About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for people with serious and life-threatening rare disorders. The company's portfolio consists of five commercialized products and multiple clinical and pre-clinical product candidates.

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 BioMarin's BMN 270 program generally and the timing and results of the clinical trial of BMN 270. 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 BMN 270, including final analysis of the above interim data; any potential adverse events observed in the continuing monitoring of the patients in the Phase 1/2 trial; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities; our ability to successfully manufacture the product candidate for the preclinical and clinical trials; 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 2015 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.

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[1] Source: National Hemophilia Foundation
http://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A

[2] Source: CDC
http://www.cdc.gov/ncbddd/hemophilia/data.html

[3] Source: World Federation of Hemophilia
http://www.wfh.org/en/resources/annual-global-survey
http://www.wfh.org/en/abd/prophylaxis/prophylaxis-administration-and-dosing-schedules

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