UK Regulatory Agency Approves Continued Enrollment in BioMarin Phase 1/2 Study of BMN 270 in Hemophilia A

Phase 1/2 Study Expected to Resume by End of 2016
Requirement for Prophylactic Corticosteroids Removed

SAN RAFAEL, Calif., Oct. 13, 2016 (GLOBE NEWSWIRE) -- BioMarin Pharmaceutical Inc. (NASDAQ:BMRN) announced today that the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom approved continued enrollment into the open-label Phase 1/2 study of BMN 270, an investigational gene therapy treatment for severe hemophilia A. BioMarin had previously announced that after enrolling the first 9 patients in the study, that dosing of patients had been suspended due to observed increases in alanine aminotransferase (ALT) levels that exceeded a pre specified threshold set by the company. Following study suspension, the company reviewed safety and efficacy data on the 9 patients with the MHRA, and based on its review, the MHRA approved resumption of the study. The agency also approved the company's proposed amendments to the study, which included eliminating the requirement for prophylactic corticosteroids and increasing potential additional enrollment from up to three additional patients to up to six additional patients.

BioMarin intends to resume enrollment in the Phase I/2 study before the end of 2016. Based on protocol amendments, three patients will be enrolled at a dose of 4×10^{13} vg/kg, and an additional three may be enrolled at this dose or the previously tested high dose of 6×10^{13} vg/kg. In the up to six additional patients, the requirement for prophylactic corticosteroids has been removed and the threshold for starting therapeutic corticosteroids has been increased. Safety and efficacy data from these patients will inform the Phase 2b study planned to begin in the second half of 2017.

"We are pleased that MHRA has approved the resumption of enrollment of the BMN 270 study, as well as the study amendments. We believe that the amendments will allow us to optimize the design of a robust Phase 2b clinical trial, which potentially could support an accelerated approval by health authorities," said Hank Fuchs, M.D., Chief Medical Officer at BioMarin. "We are grateful to the patients who are participating in this current study, and are encouraged by the results so far for this Phase 1/2 trial."

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 15 patients with severe hemophilia A 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.

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 Phase 1/2 clinical trial and anticipated Phase 2b 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; the content and timing of decisions by local and central ethics committees regarding the clinical trials; 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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