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BioMarin Announces Interim Analysis of INSPIRE Clinical Trial in Pompe Disease at 34th Annual J.P. Morgan Annual Healthcare Conference

Reveglucosidase Alfa Trends Positive in Respiratory Muscle Strength and Endurance Endpoints in Patients Previously Treated With Enzyme Replacement Therapy

SAN RAFAEL, Calif., Jan. 11, 2016 (GLOBE NEWSWIRE) -- BioMarin Pharmaceutical Inc. (Nasdaq:BMRN) today announced interim results from INSPIRE, a Phase 2 trial for reveglucosidase alfa, a fusion protein of insulin-like growth factor 2 and acid alpha-glucosidase (IGF2-GAA) being studied for the treatment of late-onset Pompe disease (LOPD). The interim efficacy and safety analysis is based on 24 patients who previously had been on treatment with the enzyme replacement therapy, alglucosidase alfa, and were switched to reveglucosidase alfa.

Investigators indicated that, while on treatment with alglucosidase alfa, the majority of the patient population were considered to have worsening of their Pompe disease over the last 12 months. At week 24, the 18 patients on treatment with reveglucosidase alfa and who completed the study demonstrated respiratory muscle improvements with a mean increase of 2.2 points from baseline in percent predicted Maximal Inspiratory Pressure (MIP) and a mean increase of 3.1 points from baseline in percent predicted Maximal Expiratory Pressure (MEP). Patients completing the study also experienced a mean improvement of 26.1 meters in 6 Minute Walk Test (6MWT). In the 14 patients who met eligibility at both screening and baseline and completed the study, a mean increase of 3.8 points from baseline in percent predicted MIP also was observed. The 18 patients completing the study showed a mean decrease of 3.7 points from baseline in percent predicted Forced Vital Capacity (FVC), but were considered relatively unchanged from screening at -0.7 points in percent predicted. BioMarin will present these data at an upcoming medical meeting.

"We are encouraged by the positive trends in respiratory muscle strength as measured by pressures, which may indicate a possible halt in decline or improvement in lung capacity and endurance in late-onset Pompe disease," said Hank Fuchs, M.D., Executive Vice President and Chief Medical Officer at BioMarin. "Reveglucosidase alfa has the potential to be an additional choice for Pompe patients, and we look forward to working with health authorities and the patient community to advance this experimental therapy to the next stage of clinical development."

"Pompe is a progressive and debilitating disease, and patients need additional treatment options. The reveglucosidase alfa data appears promising and could be a potential new enzyme replacement therapy that could make a meaningful difference to late-onset Pompe patients," said Professor Benedikt Schoser of the Friederich-Baur Institute and speaker of the German working group for Pompe disease.

TABLE 1: Reveglucosidase Alfa Interim Phase 2 Study Results

Endpoint	N	Baseline (SD)	Week 24 (SD)	Mean change from baseline to week 24 (SD)
MIP - mean % predicted	18	50.0 (17.5)	52.1 (15.9)	2.2 (8.3)
MEP - mean % predicted	18	38.9 (12.3)	42.0 (12.1)	3.1 (8.7)
6MWT - mean meters	17	345.8 (95.3)	371.9 (114.2)	26.1 (40.6)
$FVC_{upright}$ - mean % predicted	18	60.7 (15.1)	56.9 (14.2)	-3.7 (4.4)

Only patients with baseline and week 24 results are included

3.8% (6.4) absolute improvement per protocol analysis of MIP (14 patients who met eligibility at screening and baseline)

FVC change from screening -0.7%

TABLE 2: Reveglucosidase Alfa Interim Phase 2 Study Baseline Characteristics

Baseline characteristic	701-301 (N=23)*

Age — mean yrs (range)	48.5 (19-69)
Sex- M/F %	48/52
Time on alglucosidase alfa — mean years (SD)	5.5 (2.7)
MIP — mean % predicted (SD)	51.2 (17.2)
MEP — mean % predicted (SD)	40.9 (12.1)
6MWT — mean meters (SD)	317.7 (102.3)
FVC Upright — mean % predicted (SD)	60.7 (15.9)
Use of walking aids in 6MWT- %	34.8
Use of ventilatory support- %	34.8

*One patient was excluded due to inclusion violation of not being diagnosed with LOPD.

Safety

Six patients discontinued treatment early, and two patients experienced serious adverse events. Hypoglycemia was generally similar in frequency and severity as in the previous study, and the overall pattern of safety was otherwise consistent with experience using other enzyme replacement therapy.

INSPIRE Study Design

The INSPIRE clinical trial is a Phase 2 single-arm, open-label, switchover study of reveglucosidase alfa in patients with late-onset Pompe disease (LOPD) who have been receiving treatment with recombinant human acid alpha glucosidase (rhGAA) for 48 weeks or longer. This study was changed from a Phase 2/3 to a Phase 2 study to allow use of drug employing a new purification process, which could be used in an anticipated Phase 3 registration-enabling trial. All patients in the study have been transferred to the new material, and all future patients will be treated with the new material.

Ambulatory patients who have mild to moderate respiratory impairment will switch directly to receive reveglucosidase alfa 20 mg/kg by IV infusion every other week. The change in value in primary endpoint, Maximum Inspiratory Pressure (MIP), and secondary endpoint, Maximum Expiratory Pressure (MEP), Forced Vital Capacity (FVC) Upright and Six-Minute Walk Test (6MWT) will be measured as the difference between the Baseline value and the Week 24 value within each individual subject. The study has a 24-week treatment period followed by an extension period of up to 240 weeks.

About Reveglucosidase Alfa

Reveglucosidase alfa is an investigational enzyme replacement therapy for Pompe disease. It is a novel fusion protein of insulin-like growth factor 2 and acid alpha glucosidase (IGF2-GAA) designed to target delivery to the lysosomes where the enzyme is most needed. The drug replaces the enzyme (GAA) that prevents the glycogen build up that causes Pompe disease. It has a small protein attached to it (IGF-2), which allows it to attach to the surface of the muscle cell more tightly than the untagged enzyme (GAA). Research has shown that reveglucosidase alfa is able to get into the cell and clear much of the excess glycogen buildup that creates the problems in Pompe disease.

About Pompe Disease

Pompe Disease is an autosomal recessive metabolic disorder which damages muscle and nerve cells throughout the body. It is caused by an accumulation of glycogen in the lysosome due to deficiency of the lysosomal acid alpha-glucosidase enzyme. The build-up of glycogen causes progressive muscle weakness (myopathy) throughout the body and affects various body tissues, particularly in the heart, skeletal muscles, liver and nervous system. Measurement of maximal inspiratory and expiratory pressures are used to assess pulmonary muscle function. Maximal inspiratory pressure (MIP) is the maximal pressure that can be produced by the patient trying to inhale through a blocked mouthpiece. Maximal expiratory pressure (MEP) is the maximal pressure measured during forced expiration through a blocked mouthpiece after a full inhalation.

There are two main forms of Pompe disease: late onset which occurs in about one in 57,000 births and infantile onset which occurs in about one in 140,000 births. It is inherited in an autosomal recessive manner, affects males and females equally, and in most cases, both parents of an affected child are asymptomatic carriers of the disease. The overall population is believed to be 10,000 patients globally.

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 five commercialized products

and multiple clinical and pre-clinical product candidates. For additional information, please visit www.BMRN.com.

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 reveglucosidase alfa; the continued clinical development of reveglucosidase alfa; the final results of the Phase 2 trial of reveglucosidase alfa, 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 reveglucosidase alfa; the final analysis of the interim data; our ability to successfully manufacture reveglucosidase alfa; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities concerning reveglucosidase alfa; 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.

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