# BioMarin's VIMIZIM(R) (elosulfase alfa) Approved in Brazil for Treatment of Morquio A Syndrome

**VIMIZIM is First and Only Treatment in Brazil for Patients With This Ultra-Rare Genetic Condition**

SAN RAFAEL, Calif., Dec. 10, 2014 (GLOBE NEWSWIRE) -- BioMarin Pharmaceutical Inc. (Nasdaq:BMRN) today announced that the Agência Nacional de Vigilancia Sanitaria (ANVISA), or the National Health Surveillance Agency Brazil, has approved VIMIZIM® (elosulfase alfa) for the treatment of patients with mucopolysaccharidosis type IVA (MPS IVA), also known as Morquio A syndrome. This is the second country in the month of December to approve VIMIZIM, the first and only treatment for the ultra-rare genetic condition. Australia also approved the therapy on December 7, 2014.

"As a physician dedicated to the MPS community, I am delighted to have the opportunity to move my patients suffering from Morquio A syndrome beyond supportive care to a therapy that can address their condition at the cellular level and potentially change the course of the disease," said Roberto Giugliani, MD, PhD, Professor of Genetics at the Federal University of Rio Grande do Sul, Brazil. "The approval of VIMIZIM in Brazil is a significant milestone for the community of patients with Morquio A syndrome who can now receive for the first time a specific treatment for their rare condition."

Morquio A syndrome is an ultra-rare, severely debilitating disease affecting an estimated 3,000 patients in the developed world. The disease occurs as a result of a deficiency of activity in an enzyme involved in glycosaminoglycan (GAG) metabolism. The pervasive and progressive accumulation of GAGs leads to significant morbidities and multisystemic clinical impairments resulting in diminished functional capacity, impaired quality-of-life and early mortality. The most common features of the disease are progressive skeletal dysplasia, the need for frequent surgical procedures related primarily to musculoskeletal or respiratory dysfunction, and significant limitations in mobility, endurance and breathing.

"Approval in Brazil advances our vision of taking this much needed therapy worldwide a reality," said Daniela Giovannetti, Senior Director, Medical Services in Latin America. "We are grateful to the patients from all over Latin America for participating in the VIMIZIM clinical trials. Their participation is absolutely essential to the success of our development program around the world."

The U.S. Food and Drug Administration (FDA) approved the VIMIZIM license application for the treatment of patients with Morquio A syndrome on February 14, 2014. The therapy is also approved in Canada, Australia and the European Union. Marketing applications have been submitted in several other countries.

**About VIMIZIM**

VIMIZIM® (elosulfase alfa) is a treatment for patients with Morquio A syndrome, or mucopolysaccharidosis IVA (MPS IVA). VIMIZIM is the first approved enzyme replacement therapy (ERT) designed to target the underlying cause of Morquio A Syndrome—a deficiency in the enzyme N-acetylgalactosamine-6 sulfatase (GALNS). VIMIZIM is intended to provide the exogenous enzyme GALNS that will be taken up into the lysosomes and increase the catabolism of GAGs. Morquio A syndrome is a rare, severely debilitating and progressive disease that previously had no approved, standard-of-care treatment other than supportive care.

**Important Safety Information**

Life-threatening allergic reactions, known as anaphylaxis, can occur during VIMIZIM® (elosulfase alfa) infusions. Due to the potential for anaphylaxis, appropriate medical support should be readily available when VIMIZIM is administered and for an appropriate period of time following administration.

Hypersensitivity reactions have been observed as early as 30 minutes from the start of infusion but as late as six days after infusion. Frequent symptoms of hypersensitivity reactions included anaphylactic reactions, urticaria, peripheral edema, cough, dyspnea, and flushing.

Because of the potential for hypersensitivity reactions, administer antihistamines with or without antipyretics prior to infusion. If severe hypersensitivity reactions occur, immediately stop the infusion of VIMIZIM and initiate appropriate treatment. Patients with acute febrile or respiratory illness at the time of VIMIZIM infusion may be at higher risk of life-threatening complications from hypersensitivity reactions.

Sleep apnea is common in MPS IVA patients. Evaluation of airway patency should be considered prior to initiation of treatment with VIMIZIM. Patients using supplemental oxygen or continuous positive airway pressure (CPAP) during sleep should have these treatments readily available during infusion in the event of an acute

reaction, or extreme drowsiness/sleep induced by antihistamine use.

Spinal or cervical cord compression (SCC) is a known and serious complication of MPS IVA and may occur as part of the natural history of the disease. In clinical trials, SCC was observed both in patients receiving VIMIZIM and patients receiving placebo. Patients with MPS IVA should be monitored for signs and symptoms of SCC (including back pain, paralysis of limbs below the level of compression, urinary and fecal incontinence) and given appropriate clinical care.

All patients treated with VIMIZIM 2 mg/kg once per week in the placebo-controlled trial developed anti-drug antibodies.

VIMIZIM should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known if VIMIZIM is present in human milk.

Safety and effectiveness in pediatric patients below 5 years of age have not been established.

In clinical trials, the most common adverse reactions (≥10%) occurring during infusion included pyrexia, vomiting, headache, nausea, abdominal pain, chills, and fatigue. The acute reactions requiring intervention were managed by either temporarily interrupting or discontinuing infusion, and administering additional antihistamine, antipyretics, or corticosteroids.

Please see full Prescribing Information, including boxed warning, or visit www.VIMIZIM.com.

**About Morquio A Syndrome**

Morquio A syndrome, or Mucopolysaccharidosis IVA (MPS IVA) is a disease in which people are missing an enzyme essential in the breakdown and removal of the glycosaminoglycans (GAGs) called keratan sulfate (KS) and chondroitin-6-sulfate (C6S). The incompletely broken down GAGs remain stored in cells in the body causing progressive damage. This excessive storage causes systemic skeletal dysplasia, short stature, and joint abnormalities, limiting mobility and endurance. Malformation of the chest impairs respiratory function, and looseness of joints in the neck causing spinal instability and potentially spinal cord compression. Other symptoms may include hearing loss, corneal clouding, and heart disease. Initial symptoms often become evident in the first five years of life. The disease substantially limits both the quality and length of life of those affected.

The rate of incidence of Morquio A syndrome is as yet unconfirmed and varies among different populations, and estimates vary between 1 in 200,000 live births and 1 in 450,000 live births.

**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 BMN 165 (PEGylated recombinant phenylalanine ammonia lyase), also referred to as 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, 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, a modified C-natriuretic peptide, which is currently in Phase 2 clinical development for the treatment of achondroplasia, BMN 190, a recombinant human tripeptidyl peptidase-1 (rhTPP1) for the treatment of CLN2 disorder, a form of Batten disease, which is currently in Phase 1, 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: expectations regarding the marketing application filing for VIMIZIM with ANVISA; and the marketing and commercialization of VIMIZIM in Brazil. 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 clinical trials of its product candidates; any further actions by ANVISA; the outcome of pricing and reimbursement negotiations with relevant authorities in Brazil; 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 2013 Annual Report on Form 10-K, as amended, and the factors contained in BioMarin's reports on Form 8-K. 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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