Chiesi Global Rare Diseases and Protalix Biotherapeutics Acknowledge CHMP Negative Opinion on Every Four Week Dosing Regimen of Elfabrio® (pegunigalsidase alfa) in the EU

October 17, 2025

Every two weeks remains approved as a dosing regimen of Elfabrio in the EU

PARMA, Italy and CARMIEL, Israel, Oct. 17, 2025 (GLOBE NEWSWIRE) -- Chiesi Global Rare Diseases, a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people living with rare diseases, and Protalix BioTherapeutics, Inc. (NYSE American:PLX), a biopharmaceutical company focused on the development, production and commercialization of recombinant therapeutic proteins produced by its proprietary ProCellEx® plant cell-based protein expression system, acknowledge that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a negative opinion on the request to approve the dosing regimen of 2 mg/kg body weight infused every 4 weeks (E4W) for Elfabrio (pegunigalsidase alfa, in addition to the currently approved dosing regimen of 1 mg/kg body weight infused every 2 weeks (E2W).

“We are disappointed by the result of this review but want to express our immense appreciation for the collaboration of the patient community, researchers and European Commission throughout this process,” said **Giacomo Chiesi, Executive Vice President, Chiesi Global Rare Diseases**. “We are proud to be a part of this community and will continue to prioritize the potential to advance and evolve safe and effective solutions for Fabry disease with reduced treatment burden.”

"We, together with Chiesi, remain committed to reducing the treatment burden for patients with Fabry disease," said **Dror Bashan, Protalix's President and Chief Executive Officer**. "The results of this review do not change this priority. We are grateful to all of the patients and investigators, and their staff members, who participated in the every 4 weeks clinical trial programs."

“We acknowledge this outcome with disappointment but also with gratitude for the dedication shown by all involved – from patients and advocates to researchers and regulators,” said **Mary Pavlou, President of Fabry International Network (FIN).** “The Fabry International Network remains committed to fostering collaboration that drives meaningful progress both in safety and effectiveness and strives for advancements that make a real difference in daily life and long-term outcomes.”

The submission for CHMP review was based on data from an open-label, switch-over trial, BRIGHT (formally PB-102-F50), designed to assess the safety, efficacy and pharmacokinetics (PK) of pegunigalsidase alfa 2 mg/kg administered every four weeks and its ongoing open label extension study, CLI-06657AA1-03 (formerly PB-102-F51). The two studies combined have a median exposure of almost six years. Further support was provided from modelling and exposure-response analyses across prior trials (PB-102-F01/-F02, PB-102-F20, and PB-102-F50). These data were not deemed sufficient to conclude on similar efficacy. Chiesi and Protalix intend to keep working together to support the Fabry disease community.

Important Safety Information
Indication

Elfabrio® (pegunigalsidase alfa-iwxj) is indicated for the treatment of adults with confirmed Fabry disease.

Important Safety Information

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS Patients treated with Elfabrio have experienced hypersensitivity reactions, including anaphylaxis. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during Elfabrio administration. If a severe hypersensitivity reaction (eg, anaphylaxis) occurs, discontinue Elfabrio immediately and initiate appropriate medical treatment. In patients with severe hypersensitivity reaction, a desensitization procedure to Elfabrio may be considered.

Prior to Elfabrio administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. Inform patients and caregivers of the signs and symptoms of hypersensitivity reactions and infusion-associated reactions (IARs), and instruct them to seek medical care immediately if such symptoms occur.

- If a severe hypersensitivity reaction (including anaphylaxis) or severe IAR occurs, immediately discontinue Elfabrio administration and initiate appropriate medical treatment.
- If a mild to moderate hypersensitivity reaction or IAR occurs, consider slowing the infusion rate or temporarily withholding the dose.

In clinical trials, 20 (14%) Elfabrio-treated patients experienced hypersensitivity reactions. Four Elfabrio-treated patients (3%) experienced anaphylaxis reactions that occurred within 5 to 40 minutes of the start of the initial infusion. The signs and symptoms of hypersensitivity reactions and anaphylaxis included headache, nausea, vomiting, throat tightness, facial and oral edema, truncal rash, tachycardia, hypotension, rigors, urticaria, intense pruritus, moderate upper airway obstructions, macroglossia, and mild lip edema.

In clinical trials, 41 (29%) Elfabrio-treated patients experienced one or more infusion-associated reactions, including hypersensitivity, nausea, chills, pruritus, rash, chest pain, dizziness, vomiting, asthenia, pain, sneezing, dyspnea, nasal congestion, throat irritation, abdominal pain, erythema, diarrhea, burning sensation, neuralgia, headache, paresthesia, tremor, agitation, increased body temperature, flushing, bradycardia, myalgia, hypertension, and hypotension.

A case of membranoproliferative glomerulonephritis with immune depositions in the kidney was reported during clinical trials. Monitor serum creatinine

and urinary protein-to-creatinine ratio. If glomerulonephritis is suspected, discontinue treatment until a diagnostic evaluation can be conducted.

When switching to Elfabrio from a prior enzyme replacement therapy, the risk of hypersensitivity reactions and infusion-associated reactions may be increased in certain patients with pre-existing anti-drug antibodies (ADAs). Consider monitoring IgG and IgE ADAs and clinical or pharmacodynamic response (eg, plasma lyso-Gb3 levels).
The most common adverse reactions (≥15%) were infusion-associated reactions, nasopharyngitis, headache, diarrhea, fatigue, nausea, back pain, pain in extremity, and sinusitis.

Please see Full Prescribing Information for Elfabrio.

About Fabry Disease
Fabry disease is a rare, inherited lysosomal storage disorder caused by mutations in the GLA gene, which leads to a deficiency of the enzyme alpha-galactosidase A. This deficiency results in an accumulation of a fatty substance called globotriaosylceramide (GL-3) in the body's cells, affecting the heart, kidneys, skin, nervous system, and other organs. Fabry disease can cause a range of serious signs and symptoms, including fatigue, chronic pain, gastrointestinal issues, decreased ability to sweat, progressive kidney failure, heart complications, and increased risk of stroke.

The condition affects both males and females and can present from childhood through adulthood, often with delayed diagnosis or misdiagnosis. While Fabry disease is rare, early detection and access to appropriate treatment — such as enzyme replacement therapy or pharmacological chaperones — are critical in managing symptoms and slowing disease progression.

About Chiesi Group
Chiesi is a research-oriented international biopharmaceutical group that develops and markets innovative therapeutic solutions in respiratory health, rare diseases, and specialty care. The company's mission is to improve people's quality of life and act responsibly towards both the community and the environment.

By changing its legal status to a Benefit Corporation in Italy, the US, France and Colombia, Chiesi's commitment to creating shared value for society as a whole is legally binding and central to company-wide decision-making. As a certified B Corp since 2019, Chiesi is part of a global community of businesses that meet high standards of social and environmental impact. The company aims to reach Net-Zero greenhouse gases (GHG) emissions by 2035.
With 90 years of experience, Chiesi is headquartered in Parma (Italy), with 31 affiliates worldwide, and counts more than 7,500 employees. The Group's research and development center in Parma works alongside 6 other important R&D hubs in France, the US, Canada, China, the UK, and Sweden.

For more information visit www.chiesi.com.

About Chiesi Global Rare Diseases
Chiesi Global Rare Diseases is a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people living with rare diseases. As a family business, Chiesi Group strives to create a world where it is common to have therapy for all diseases and acts as a force for good, for society and the planet. The goal of the Global Rare Diseases unit is to ensure equal access so as many people as possible can experience their most fulfilling life. The unit collaborates with the rare disease community around the globe to bring voice to underserved people in the health care system.

For more information visit www.chiesirarediseases.com.

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About Protalix BioTherapeutics, Inc.
Protalix is a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins expressed through its proprietary plant cell-based expression system, ProCellEx. It is the first company to gain U.S. Food and Drug Administration (FDA) approval of a protein produced through plant cell-based in suspension expression system. This unique expression system represents a new method for developing recombinant proteins in an industrial-scale manner. Protalix has licensed to Pfizer Inc. the worldwide development and commercialization rights to taliglucerase alfa for the treatment of Gaucher disease, Protalix's first product manufactured through ProCellEx, excluding in Brazil, where Protalix retains full rights. Protalix's second product, Elfabrio®, was approved by both the FDA and the European Medicines Agency in May 2023.

Protalix has partnered with Chiesi Farmaceutici S.p.A. for the global development and commercialization of Elfabrio. Protalix's development pipeline consists of proprietary versions of recombinant therapeutic proteins that target established pharmaceutical markets, including the following product candidates: PRX–115, a plant cell-expressed recombinant PEGylated uricase for the treatment of uncontrolled gout; PRX–119, a plant cell-expressed long acting DNase I for the treatment of NETs-related diseases; and others.

Protalix BioTherapeutics, Inc. Forward-Looking Statements
To the extent that statements in this press release are not strictly historical, all such statements are forward-looking, and are made pursuant to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. The terms "anticipate," "believe," "estimate," "expect," "can," "continue," "could," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" and other words or phrases of similar import are intended to identify forward-looking statements. These forward-looking statements are subject to known and unknown risks and uncertainties that may cause actual future experience and results to differ materially from the statements made. These statements are based on our current beliefs and expectations as to such future outcomes. Drug discovery and development involve a high degree of risk and the final results of a clinical trial may be different than the preliminary findings for the clinical trial. Factors that might cause material differences include, among others: risks related to the commercialization of Elfabrio; risks relating to Elfabrio market acceptance, competition, reimbursement and regulatory actions, including as a result of the boxed warning contained in the FDA approval received for the product; the possible disruption of Protalix's operations due to the war declared by Israel's security cabinet against the Hamas terrorist organization located in the Gaza Strip, the military campaign against the Hezbollah and other terrorist activities and armed conflict, including as a result of the disruption of the operations of certain regulatory authorities and of certain of Protalix's suppliers, collaborative partners, licensees, clinical trial sites, distributors and customers, and the risk that the current hostilities will result in a greater regional conflict; delays in the approval or potential rejection of any applications filed with the FDA, EMA or other health regulatory authorities for Protalix's product candidates, and other risks relating to the review process; the risk that the results of clinical trials will not support the applicable claims of safety or efficacy; risks related to the amount and sufficiency of Protalix's cash and cash equivalents; risks relating to changes to published interim, topline or preliminary data from clinical trials; the inherent risks and uncertainties in developing drug platforms and products of the type we are developing; the impact of development of competing therapies and/or technologies by other companies; and risks relating to changes in healthcare laws, rules and regulations in the United States or elsewhere; and other factors described in our filings with the U.S. Securities and Exchange Commission. The statements in this press release are valid only as of the date hereof and Protalix disclaims any obligation to update this information, except as may be required by law.

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