Chiesi Global Rare Diseases and Protalix BioTherapeutics Announce FDA Approval of ELFABRIO® (pegunigalsidase alfa-iwxj) for the Treatment of Fabry Disease

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- PEGylated enzyme replacement therapy designed to provide long half-life -*

BOSTON and CARMIEL, Israel, May 10, 2023 /PRNewswire/ -- Chiesi Global Rare Diseases, a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people affected by rare diseases, and Protalix BioTherapeutics, Inc. (NYSE American:PLX), a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins expressed through its proprietary plant cell-based expression system, ProCellEx®, announced today that the U.S. Food and Drug Administration (FDA) has approved ELFABRIO (pegunigalsidase alfa-iwxj) in the United States for the treatment of adult patients with Fabry disease.

"*While much progress has been made in the treatment of Fabry disease, there is still a need for new treatment options,"* said **Giacomo Chiesi, head of Chiesi Global Rare Diseases**. "*We established Chiesi Global Rare Diseases to deliver innovative therapies and solutions for people affected by rare diseases. With the FDA approval of ELFABRIO, we can now offer people living with Fabry disease an alternative treatment option*."

"*We are extremely pleased to receive FDA approval of ELFABRIO for the treatment of adult patients with Fabry disease*," said **Dror Bashan, Protalix's President and Chief Executive Officer**. "*This approval is a testament to the dedication of the Protalix and Chiesi teams to deliver this much needed new therapeutic option to patients in need. The totality of clinical data suggests that ELFABRIO has the potential to be a long-lasting therapy. Together with Chiesi, we are grateful to all of the patients and investigators and their staff members who participated in our clinical trial programs and remain committed to bringing ELFABRIO to patients with Fabry disease*."

ELFABRIO is a PEGylated enzyme replacement therapy (ERT). It is a recombinant human α–Galactosidase–A enzyme expressed in plant-cell culture that is designed to provide a long half-life.

The safety, tolerability, and efficacy of ELFABRIO has been studied in a comprehensive clinical development program in more than 140 patients with up to 7.5 years of follow up treatment. It has been studied in both ERT-naïve and ERT-experienced patients, including a head-to-head trial that met its primary endpoint with ELFABRIO demonstrating non-inferior efficacy to agalsidase beta in controlling estimated glomerular filtration rate (eGFR) decline, and in which ELFABRIO was generally well-tolerated with the majority of adverse events being mild or moderate in severity.

"It is important to understand that there is a lot of variability in Fabry disease and misdiagnoses are common, especially in women," said **Jack Johnson, founder of the Fabry Support & Information Group (FSIG).** "Growing up, a lot of people didn't know what was wrong with me. They knew I was different, but they didn't know why. Now we have made advances in screening, treatment, and monitoring for Fabry disease."

*ELFABRIO has an initial half-life of 78.9 ± 10.3 hours. Clinical studies have not established that half-life results in superior efficacy or safety based on clinically relevant end points.

Indication and 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 an X–linked inherited disease that results from deficient activity of the lysosomal α–Galactosidase–A enzyme resulting in progressive accumulation of abnormal deposits of a fatty substance called globotriaosylceramide (Gb_3) in the lysosomes throughout a person's body. Fabry disease occurs in one person per 40,000 to 60,000. Fabry patients inherit a deficiency of the α–Galactosidase–A enzyme, which is normally responsible for the breakdown of Gb_3. The abnormal storage of Gb_3 increases with time and, accordingly, Gb_3 accumulates, primarily in the blood vessel and tissues. The ultimate consequences of Gb_3 deposition range from episodes of pain and impaired peripheral sensation to end-organ failure.

About ELFABRIO

ELFABRIO (pegunigalsidase alfa-iwxj), a PEGylated enzyme replacement therapy (ERT) to treat Fabry disease, is a plant cell culture-expressed, and chemically modified stabilized recombinant version of the α–Galactosidase–A enzyme. Protein sub-units are covalently bound via chemical cross-linking using short PEG moieties, resulting in a molecule with stable pharmacokinetic parameters. In clinical studies, ELFABRIO has been observed to have an initial half-life of 78.9 ± 10.3 hours. Clinical studies have not established that half-life results in superior efficacy or safety based on clinically relevant end points.

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 affected by rare diseases. As a family business, Chiesi Group strives to create a world where it is common to have a 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.

About Chiesi Group

Chiesi is an international, research-focused biopharmaceuticals 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, and France, Chiesi's commitment to create shared value for society as a whole is legally binding and central to company-wide decision-making. As a certified B Corp since 2019, we're 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 over 85 years of experience, Chiesi is headquartered in Parma (Italy), operates in 31 countries, and counts more than 6,500 employees. The Group's research and development centre in Parma works alongside 6 other important R&D hubs in France, the US, Canada, China, the UK, and Sweden.

For further information please visit www.chiesi.com.

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 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, Protalix's first product manufactured through ProCellEx, excluding in Brazil, where Protalix retains full rights.

Protalix's development pipeline consists of proprietary versions of recombinant therapeutic proteins that target established pharmaceutical markets, including the following product candidates: pegunigalsidase alfa, a modified stabilized version of the recombinant human α-Galactosidase-A protein for the treatment of Fabry disease; PRX–115, a plant cell-expressed recombinant PEGylated uricase for the treatment of severe gout; PRX–119, a plant cell-expressed long action DNase I for the treatment of NETs-related diseases; and others. Protalix has partnered with Chiesi Farmaceutici S.p.A., both in the United States and outside the United States, for the development and commercialization of pegunigalsidase alfa-iwxj.

Protalix's 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 "expect," "anticipate," "believe," "estimate," "project," "may," "plan," "will," "would," "should" and "intend," 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 Protalix's current beliefs and expectations as to such future outcomes. Factors that might cause material differences include, among others: risks related to the commercialization of ELFABRIO; the likelihood that the FDA, European Medicines Agency (EMA) or other applicable health regulatory authorities will approve an alternative dosing regimen for ELFABRIO; risks related to the commercial success of Protalix's other product and product candidates, if approved; failure or delay in the commencement or completion of preclinical studies and clinical trials of our other product candidates which may be caused by several factors, including: slower than expected rates of patient recruitment; unforeseen safety issues; determination of dosing issues; lack of effectiveness during clinical trials; inability to satisfactorily demonstrate non-inferiority to approved therapies; inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; and inability to monitor patients adequately during or after treatment; delays in the approval or potential rejection of any applications we file with the FDA, EMA or other health regulatory authorities for our other product candidates, and other risks relating to the review process; risks associated with the novel coronavirus disease, or COVID–19, outbreak, which may adversely impact our business, preclinical studies and clinical trials; the risk that the results of the clinical trials of our product candidates will not support the applicable claims of safety or efficacy, or that our product candidates will not have the desired effects or will be associated with undesirable side effects or other unexpected characteristics; risks related to our ability to maintain and manage our relationship with our collaborators, distributors or partners; our dependence on performance by third party providers of services and supplies, including without limitation, clinical trial services; 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 institutions; potential product liability risks, and risks of securing adequate levels of product liability and other necessary insurance coverage; 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 we disclaim any obligation to update this information, except as may be required by law.

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