Protalix BioTherapeutics and Chiesi Global Rare Diseases Announce the Submission of a Marketing Authorization Application to the European Medicines Agency for PRX-102 for the Treatment of Fabry Disease

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CARMIEL, Israel and BOSTON, Feb. 24, 2022 /PRNewswire/ -- Protalix BioTherapeutics, Inc. (NYSE: PLX) (TASE: 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, and Chiesi Global Rare Diseases, a business unit of Chiesi Farmaceutici S.p.A., an international research-focused healthcare Group (Chiesi Group), today announced the submission of a Marketing Authorization Application (MAA) via centralized procedure to the European Medicines Agency (EMA) for pegunigalsidase alfa (PRX–102) for the proposed treatment of adults with Fabry disease, and the subsequent validation of the MAA by the EMA.

The MAA submission includes a comprehensive set of preclinical, clinical and manufacturing data compiled from the Company's completed and ongoing clinical studies evaluating PRX–102 as a potential treatment for Fabry disease. The submission is supported by the 12–month interim data analysis generated from the phase III BALANCE clinical trial, which was released in June 2021. Data generated from the completed phase III BRIDGE clinical trial, the phase 1/2 clinical trial in naive or untreated patients, and from the related extension studies with 1 mg/kg every two weeks were also included in the filing. In addition, the MAA includes data from the completed 12–month switch–over phase III BRIGHT clinical trial of patients treated with the 2 mg/kg every 4 weeks dosage.

"The submission marks a considerable accomplishment in the development of PRX–102 and is an important step forward in navigating regulatory channels in the European Union. This centralized procedure via the EMA allows for the submission of a single marketing authorization application to the European Union, and, if approved, allows Chiesi, our commercial partner, to market and make PRX–102 available to patients and healthcare professionals across the entire European Union," said Dror Bashan, Protalix's President and Chief Executive Officer. "We are committed to bringing PRX–102 to market and look forward to providing an alternative treatment option for people with Fabry disease."

The scientific evaluation will be conducted by the Committee for Medicinal Products for Human Use (CHMP) with predefined assessment milestones. At the completion of the review, the CHMP will issue a scientific opinion on whether PRX-102 may be authorized or not. The EMA will forward this opinion to the European Commission, which is expected to adopt the EMA's scientific opinion.

"Our team at Chiesi is deeply committed to the Fabry disease community and we are grateful to the patients and investigators who have helped us better understand the unmet treatment needs and whose participation in the clinical trials has led us to this important milestone," said Giacomo Chiesi, Head of Chiesi Global Rare Diseases. "We believe that the safety and efficacy data demonstrated by PRX-102 in clinical trials strongly supports this application and we look forward to completing the final stages of regulatory review."

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 blood vessel walls 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 and in the blood vessel walls. The ultimate consequences of Gb_3 deposition range from episodes of pain and impaired peripheral sensation to end–organ failure – particularly of the kidneys, but also of the heart and the cerebrovascular system.

About Pegunigalsidase Alfa (PRX–102)

Pegunigalsidase alfa (PRX–102) is an investigational, plant cell culture-expressed, and chemically modified stabilized version of the recombinant α–Galactosidase–A enzyme. Protein sub-units are covalently bound via chemical cross-linking using short PEG moieties, resulting in a molecule with unique pharmacokinetic parameters. In clinical studies, PRX–102 has been observed to have a circulatory half-life of approximately 80 hours. Protalix designed PRX–102 to potentially address the continued unmet clinical need in Fabry patients.

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. Protalix was 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. Protalix's unique expression system represents a new method for developing recombinant proteins in an industrial-scale manner.

Protalix's first product manufactured by ProCellEx, taliglucerase alfa, was approved by the FDA in May 2012 and, subsequently, by the regulatory

authorities of other countries. Protalix has licensed to Pfizer Inc. the worldwide development and commercialization rights for taliglucerase alfa, excluding 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; alidornase alfa or PRX–110, for the treatment of various human respiratory diseases or conditions; PRX–115, a plant cell-expressed recombinant PEGylated uricase for the treatment of refractory 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.

About Chiesi Global Rare Diseases

Chiesi Global Rare Diseases is a business unit of the Chiesi Group established in February 2020 and focused on research and development of treatments for rare and ultra-rare disorders. The Global Rare Diseases unit works in collaboration with Chiesi Group to harness the full resources and capabilities of our global network to bring innovative new treatment options to people living with rare diseases, many of whom have limited or no treatments available. The unit is also a dedicated partner with global leaders in patient advocacy, research and patient care. For more information visit www.chiesiglobalrarediseases.com.

About Chiesi Group

Based in Parma, Italy, Chiesi is an international research-focused pharmaceuticals and healthcare group with over 85 years' experience, operating in 30 countries with more than 6,000 employees (Chiesi Group). To achieve its mission of improving people's quality of life by acting responsibly towards society and the environment, the Group researches, develops and markets innovative therapeutic solutions in its three focus areas: AIR (products and services that promote respiration, from new-born to adult populations), RARE (treatment for patients with rare and ultra-rare diseases) and CARE (products and services that support specialty care and consumer-facing self-care). The Group's Research and Development centre is based in Parma and works alongside 6 other important research and development hubs in France, the U.S., Canada, China, the UK, and Sweden to pursue its pre-clinical, clinical, and regulatory programmes. In 2018 Chiesi has changed its legal status to a Benefit Corporation, according to the law in Italy, USA and, more recently, in France, by incorporating common benefit objectives into its bylaws, to generate value for its business, for the society and the environment. Since 2019, Chiesi has been the world's largest B Corp certified pharmaceutical group. B Corps are global leaders convinced to leverage business as a force for good. Moreover, as a Benefit Corporation, Chiesi Farmaceutici S.p.A. is required by law to report annually in a transparent way about its progress in achieving the common benefits objectives it has set forward. The Group is committed to becoming carbon neutral by the end of 2035.

For more information, please visit www.chiesi.com.

Protalix BioTherapeutics Forward-Looking Statements Disclaimer

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 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 FDA's positions as conveyed in the Type A meeting minutes; risks related to the timing and progress of the preparation of a BLA resubmission addressing the complete response letter; risks related to the timing, progress and likelihood of final approval by the FDA and EMA of a resubmitted BLA and the MAA, respectively, for PRX–102 and, if approved, whether the use of PRX–102 will be commercially successful; failure or delay in the commencement or completion of our preclinical studies and clinical trials, 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 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; risks related to any transactions we may effect in the public or private equity markets to raise capital to finance future research and development activities, general and administrative expenses and working capital; 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; risks related to the amount and sufficiency of our cash and cash equivalents; risks relating to our ability to make scheduled payments of the principal of, to pay interest on or to refinance our outstanding notes or any other indebtedness; our dependence on performance by third party providers of services and supplies, including without limitation, clinical trial services; delays in our preparation and filing of applications for regulatory approval; 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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