Protalix BioTherapeutics and Chiesi Global Rare Diseases Announce Final Results of the BRIGHT Phase III Clinical Trial Evaluating PRX-102 for the Treatment of Fabry Disease

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Study achieved key objectives for safety, efficacy and pharmacokinetics
After completion of the study, all patients enrolled in an extension study
Treatment with PRX-102 provided coverage for the entire four-week period between infusions
No patients developed treatment-induced anti-drug antibodies to PRX-102

CARMIEL, Israel and BOSTON, March 18, 2022 /PRNewswire/ -- Protalix BioTherapeutics, Inc. (NYSE American: 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 final results from the BRIGHT Phase III clinical trial evaluating pegunigalsidase alfa (PRX-102) for the potential treatment of Fabry disease. The results indicate that treatment with 2 mg/kg of PRX-102 administered by intravenous (IV) infusion every four weeks was well tolerated, and Fabry disease assessed by estimated glomerular filtration rate (eGFR) slope and plasma lyso-Gb_3 concentration was stable.

"We are excited to share the final data from the BRIGHT study, an important milestone in the progress of our PRX-102 clinical program," said Dror Bashan, Protalix's President and Chief Executive Officer. "The availability of this data for review by the U.S. Food and Drug Administration, the European Medicines Agency and other regulators is another step forward towards the anticipated approval of PRX-102 as a potential good alternative for adult Fabry patients in both the regular 1 mg\kg every two weeks as well as the 2 mg\kg every four weeks regimen."

PRX-102 is a plant cell-expressed recombinant, PEGylated, cross-linked α-galactosidase-A product candidate. The BRIGHT Phase III clinical trial (NCT03180840) was a multicenter, multinational open-label, switch-over study designed to evaluate the safety, efficacy and pharmacokinetics of treatment with 2 mg/kg of PRX-102 administered every four weeks for 52 weeks (a total of 14 infusions). The study enrolled 30 adult patients with Fabry disease (24 males and 6 females) with mean (SD) age of 40.5 (11.3) years, ranging from 19 to 58 years, who previously received an approved enzyme replacement therapy (ERT) for at least three years on a stable dose administered every two weeks (agalsidase alfa – Replagal® or agalsidase beta – Fabrazyme®). The most common Fabry disease symptoms at baseline were acroparesthesia, heat intolerance, angiokeratomas and hypohydrosis.

All patients who participated in the study received at least one dose of PRX-102, and 29 patients completed the study. Of these 29 patients, 28 received the intended regimen of 2 mg/kg of PRX-102 every four weeks throughout the entire study, while one patient was switched to 1 mg/kg of PRX-102 every two weeks per protocol at the 11^{th} infusion. One patient withdrew from the study after the first infusion due to a traffic accident.

First infusions of PRX-102 were administered under controlled conditions at the investigational site. Based on pre-specified criteria in the study protocol, patients were able to receive their PRX-102 infusions at a home care setup once the Investigator and Sponsor Medical Monitor agreed that it was safe to do so.

Overall, 33 of 182 total treatment-emergent adverse events (TEAEs) reported in nine (30.0%) patients were considered treatment-related; all were mild or moderate in severity and the majority were resolved at the end of the study. There were no serious or severe treatment-related TEAEs and no TEAEs led to death or study withdrawal. Of the treatment-related TEAEs, 27 were infusion-related reactions (IRRs) and the remainder were single events of diarrhea, erythema, fatigue, influenza-like illness, increased urine protein/creatinine ratio, and urine positive for white blood cells. The 27 IRRs were reported in five (16.7%) patients, all male. All IRRs occurred during the infusion or within two hours post-infusion; no events were recorded between two and 24 hours post-infusion. None of the patients without anti-drug antibodies (ADAs) at screening developed treatment-induced ADAs following the switch to PRX-102 treatment.

Study outcome measures show that plasma lyso-Gb_3 concentrations remained stable during the study with a mean change (±SE) of 3.01 nM (0.94) from baseline (19.36 nM ±3.35) to Week 52 (22.23 ±3.60 nM). Mean absolute eGFR values were stable during the 52-week treatment period, with a mean change from baseline of -1.27 mL/min/1.73 m^2(1.39). Mean (SE) eGFR slope, at the end of the study, for the overall population, was -2.92 (1.05) mL/min/1.73m^2/year indicating stability.

"We are pleased to announce final results from the BRIGHT Phase III clinical trial and would like to thank the study investigators, Fabry disease patients, and their families who dedicated their time and efforts to this significant research," said Giacomo Chiesi, head of Chiesi Global Rare Diseases. "Based on these data and additional clinical studies, we believe PRX-102 may be an important new treatment option for patients who are currently receiving ERT infusions every two weeks, and we look forward to advancing our work around the world to obtain regulatory approvals as quickly as possible and provide access to the Fabry disease community."

Additional long-term data is being collected as part of an extension study (NCT03614234). The companies intend to present final data from the BRIGHT Phase III clinical trial at one or more medical conferences.

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. The Company 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.

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 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 timing and progress of the preparation of a Biologics License Application (BLA) resubmission addressing the complete response letter; risks related to the timing, progress and likelihood of final approval by the FDA and European Medicines Agency (EMA) of a resubmitted BLA and of a Marketing Authorization Application, respectively, for PRX-102 and, if approved, whether the use of PRX-102 will be commercially successful; likelihood that the FDA, EMA or other applicable health regulatory authorities will approve an alternative dosing regimen; 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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