Protalix BioTherapeutics and Chiesi Global Rare Diseases Announce Positive Topline Results from BRIGHT Phase III Open-Label, Switch-Over Clinical Trial Evaluating Pegunigalsidase Alfa 2 mg/kg every Four Weeks for 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
pegunigalsidase alfa (PRX-102) provided coverage to patients for the entire 4-week period in treated patients
No new patients developed treatment-induced anti-drug antibodies following switch to PRX-102
Third clinical study to demonstrate positive outcome in support of PRX-102, with data from PB-102-F01 and F02 Phase I/II clinical trials and BRIDGE studies previously announced

CARMIEL, Israel, Feb. 23, 2021 /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 positive topline results from the BRIGHT Phase III clinical trial evaluating pegunigalsidase alfa (PRX–102), 2 mg/kg, administered every four weeks, for the potential treatment of Fabry disease. PRX–102 is the Company's plant cell-expressed recombinant, PEGylated, cross-linked α–galactosidase–A product candidate.

The BRIGHT study is a Phase III 12-month, open-label, switch-over study designed to evaluate the safety, efficacy and pharmacokinetics of PRX–102 treatment, 2 mg/kg every four weeks, in up to 30 patients with Fabry disease previously treated with a commercially available enzyme replacement therapy (ERT) (agalsidase alfa – Replagal® or agalsidase beta – Fabrazyme®), for at least three years and on a stable dose administered every two weeks.

Topline results indicate that 2 mg/kg of PRX–102 administered by intravenous infusion every four weeks was found to be well tolerated among treated patients, and stable clinical presentation was maintained in adult Fabry patients. No new patients developed treatment-induced anti-drug antibodies (ADA) following the switch to PRX–102 treatment.

"We are excited to share these topline results from the BRIGHT study, our third consecutive positive clinical trial of PRX–102, following the Phase I/II and the BRIDGE clinical studies. The results indicate that this investigational therapy is well tolerated and potentially an effective treatment for adult patients living with Fabry disease," said Einat Brill Almon, Ph.D., Protalix's Senior Vice President and Chief Development Officer. "We are encouraged to see that all of the patients who completed this study chose to enroll in the long-term extension study. Currently, 80% of the patients enrolled in the BRIGHT study have been treated with this treatment regimen for over two years. We look forward to advancing this study and further evaluating the results."

"These results demonstrate the potential of PRX–102 to be an important treatment option for the Fabry community and that the 2 mg/kg of PRX–102 every four weeks regimen may offer meaningful benefits to both patients and physicians. Treating physicians will be empowered with a potential additional treatment regimen, shown to be well tolerated, that they can offer to Fabry patients, pending approval of PRX-102," said Dror Bashan, Protalix's President and Chief Executive Officer. "We are gratified to have a strong balance sheet supporting our development efforts and look forward to executing and delivering on a year rich with value enhancing milestones."

The BRIGHT study enrolled 30 adult patients (24 males and 6 females). The most common Fabry disease symptoms were acroparesthesia, heat intolerance, angiokeratomas and hypohydrosis. All 30 patients received at least one dose of PRX–102, and 29 patients (mean [SD] age was 40.5 [11.3] years, ranging from 19 to 58 years) completed the 12-month study. Of these 29 patients, 28 received the intended regimen of 2 mg/kg every four weeks throughout the study, while one patient was switched to PRX–102 1 mg/kg every two weeks per protocol. One patient withdrew from the study after the first infusion due to a traffic accident.

Following screening, patients were enrolled and switched from their then current ERT to intravenous (IV) infusions of 2 mg/kg of PRX–102 every four weeks for 52 weeks (a total of 14 infusions). First infusions of PRX-102 were administered under controlled conditions at the investigation site. Based on the protocol-specified criteria, 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. Safety and efficacy exploratory endpoints were assessed throughout the 52-week study.

Study outcome measures showed plasma lyso–Gb_3 concentrations remained stable during the study with a mean change of 3.01 nM from baseline (19.36 nM) to Week 52 (22.23 nM). Mean absolute change of 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.

"Patients participating in the BRIGHT study have expressed their satisfaction with the once every four weeks regimen," said John Bernat, M.D., Ph.D., University of Iowa and a Principal Investigator in the BRIGHT study. "Infusions of 2 mg/kg once every four weeks has the potential to enable patients to maintain their clinical status while reducing their number of treatments by half."

Following a survey of participants using the Quality of Life EQ-5D-5L questionnaire, responses indicate that patient perception of their own health remained high and stable throughout the 52–week study duration, with overall health mean (SE) scores of 78.3 (3.1) and 82.1 (2.9) at baseline and Week 52, respectively, in a 0 to 100 scale. Using the short-form Brief Pain Inventory (BPI) questionnaire, approximately 75% of study participants had an improvement or no change in average pain severity at Week 52 (compared to baseline). The short-form BPI interference items also remained stable during the study. Pain-related results indicate that there was no increase and/or relapse in pain. No Fabry clinical events were reported during the study.

"Of the 30 patients enrolled, 20 patients remained negative for anti-drug antibodies throughout the course of treatment. Of the 10 patients who were initially positive for anti-drug antibodies, four became negative for neutralizing antibodies at 12 months, suggesting tolerization by these patients," added Dr. Almon. "We find this immunogenicity data very encouraging and supportive to the positive benefit-risk profile of PRX–102."

"On behalf of our team at Chiesi, we are grateful to the patients, families, and investigators for their time and participation in this study," said Giacomo Chiesi, head of Chiesi Global Rare Diseases. "Their dedication has helped move this Phase III program forward and these topline data are another important milestone in our collected effort to make PRX–102 available to Fabry patients in need as rapidly as possible."

The Company intends to report final data on the BRIGHT study in the second half of 2021, and to present these findings at an appropriate medical conference.

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 PRX-102

PRX–102 (pegunigalsidase alfa) 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 for marketing 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 version of the recombinant human α–Galactosidase–A protein for the proposed treatment of Fabry disease; OPRX–106, an orally–delivered anti-inflammatory treatment; 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 gout; 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, and with SarcoMed USA, Inc. for the worldwide development and commercialization of PRX–110 for use in the treatment of any human respiratory disease or condition including, but not limited to, sarcoidosis, pulmonary fibrosis, and other related diseases via inhaled delivery.

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 Farmaceutici is an international research-focused healthcare group with 85 years of experience in the pharmaceutical industry and a global presence in 29 countries. Chiesi researches, develops, and markets innovative drugs in the respiratory therapeutics, specialist medicine, and rare disease areas. Its R&D organization is headquartered in Parma (Italy), and is integrated with R&D groups in France, the USA, the UK, and Sweden to advance Chiesi's pre-clinical, clinical, and registration programs. Chiesi employs nearly 6,000 people.

Chiesi Group is a certified Benefit corporation. 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: failure or delay in the commencement or completion of our preclinical and clinical trials which may be caused by several factors, including: risks that the FDA will not accept an application for accelerated approval of PRX–102 with the data generated to date or will request additional data or other conditions of our submission of any application for accelerated approval of PRX–102; unforeseen safety issues; determination of dosing issues; lack of effectiveness during clinical trials; inability to monitor patients adequately during or after treatment; inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; and slower than expected rates of patient recruitment; risks associated with the novel coronavirus disease (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 our claims of safety or efficacy, 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; delays in the approval or potential rejection of any applications we file with the FDA or other health regulatory authorities, and other risks relating to the review process; 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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