Protalix Biotherapeutics and Chiesi Global Rare Diseases Provide Update Regarding Clinical Development of PRX-102 for Treatment of Fabry Disease

June 2, 2021

Companies Announce Topline Results from Interim Analysis of Phase III BALANCE Clinical Trial
Protalix management to host conference call and live webcast today at 8:30 am EDT

CARMIEL, Israel and BOSTON, June 2, 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 healthare Group (Chiesi Group), today provided an update regarding the clinical development of pegunigalsidase alfa (PRX–102) for the proposed treatment of Fabry disease.

Conference Call

Protalix will host a conference call today, June 2, 2021, at 8:30 am Eastern Daylight Time, to review regulatory matters related to the development of PRX-102. To participate in the conference call, please dial the following numbers prior to the start of the call:

Conference Call Details:

Wednesday, June 2, 2021, 8:30 am Eastern Daylight Time (EDT)
Domestic: 1-877-423-9813
International: 1-201-689-8573
Conference ID: 13720271

The conference call will also be webcast live from the Protalix website and will be available via the following links:

Webcast Details:

Company Link: https://protalixbiotherapeutics.gcs-web.com/events0
Webcast Link: https://tinyurl.com/42857k4w
Conference ID: 13720271

Please access the websites at least 15 minutes ahead of the conference to register, download and install any necessary audio software.

PRX-102 Development Program Update

PRX–102 is currently being studied in the pivotal Phase III BALANCE clinical trial and in two ongoing long-term extension studies, all of which are part of the overall clinical development of PRX–102 for the proposed treatment of Fabry disease. The BALANCE study is a 24–month, randomized, double-blind, active control study of PRX–102 in Fabry patients with impaired renal function and is designed to evaluate the safety and efficacy of 1 mg/kg of PRX–102 dosed every two weeks compared to agalsidase beta (Fabrazyme®). The study enrolled 78 patients who were randomized on a 2:1 scheme. The BALANCE study is ongoing and assignment to treatment arm remains blinded.

The primary endpoint of the interim analysis is the comparison of mean annualized changes (slope) of the eGFR $_{(CKD-EPI)}$ after completion of at least 12 months of treatment between the two treatment arms. The interim efficacy analysis was conducted on two pre-defined analysis sets: Intention to Treat (ITT), consisting of all randomized patients who received at least one dose (77 patients), considered as the primary analysis for this interim review; and the Per Protocol (PP), consisting of all patients who completed at least 12 months of treatment with no major protocol violations (74 patients). The patient population (ITT analysis set) of the study is comprised of 47 males (61%) and 30 females (39%) with a mean age of 44.3 years.

The initial top-line results show that the lower boundary of the confidence interval for the mean difference between the two treatments was below the non-inferiority margin pre-specified for this interim analysis in the ITT analysis set and above such limit in the PP analysis set. At the time of this analysis, two patients discontinued participation due to treatment emergent adverse events (TEAEs). Of these two patients, one discontinued participation due to a related adverse event. No deaths were registered. Overall, safety data appears favorable and consistent with what was observed in previous clinical studies with PRX-102. Unblinded final data is anticipated to be released in the second quarter of 2022 after all remaining patients have completed the 24-month treatment period.

Based on the interim analysis of the 12-month data generated from the BALANCE study, and in combination with previously reported positive data

from the Phase III BRIGHT and BRIDGE clinical trials of PRX–102, Protalix and Chiesi intend to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for the review of PRX–102 for the proposed treatment of Fabry disease.

"We look forward to submission of the MAA to EMA for the European Union and to continuing to work with the FDA toward approval in the United States," said Dror Bashan, Protalix's President and Chief Executive Officer. "These regulatory milestones are currently our primary focus."

"The BALANCE study continues as planned through its 24-month treatment duration to support its final analysis. Based on the entire clinical development program, which includes the BRIGHT and BRIDGE studies, we believe that PRX–102 has the potential to become an important treatment option for both male and female Fabry patients. The BRIGHT and BRIDGE studies have been completed and the studies met the defined endpoints," continued Mr. Bashan.

In addition to the BALANCE study, the PRX-102 clinical program currently includes extension studies for patients who completed the BRIDGE, BRIGHT and BALANCE studies, as well as a Phase I/II clinical trial of PRX–102. Currently, more than 100 patients who participated in such studies continue to be treated in the extension studies, and additional patients completing the BALANCE study are expected to join the extension studies.

"We thank the patients and clinicians participating in our completed and ongoing clinical studies evaluating PRX-102. As we plan for MAA submission in the EU, we remain committed to advancing our development program for PRX-102 in the United States while also making access to therapy available to eligible patients through our U.S. expanded access program," said Giacomo Chiesi, head of Chiesi Global Rare Diseases.

Regarding the regulatory process in the United States, Protalix and Chiesi plan to submit a Type–A meeting request with the FDA to discuss the path for approval of PRX–102.

About Pegunigalsidase Alfa (PRX–102)

Pegunigalsidase alfa (PRX–102) is an investigational, plant cell culture-expressed, and chemically modified stabilized version of the recombinant a-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 a-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, 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.

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 timing and progress of the preparation of an updated BLA addressing the complete response letter; risks related to the timing, progress and likelihood of final approval by the FDA of a resubmitted BLA 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, 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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