Protalix BioTherapeutics and Chiesi Group Complete Enrollment in the Third Phase III Clinical Trial of pegunigalsidase alfa (PRX-102) for the Treatment of Fabry Disease

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Phase III BALANCE study now fully enrolled

BLA submission anticipated in Q1 2020 through FDA accelerated approval pathway

CARMIEL, Israel, Sept. 24, 2019 /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 its development and commercialization partner, Chiesi Farmaceutici S.p.A., an international research-focused healthcare Group (Chiesi Group), today announced the completion of enrollment in their Phase III BALANCE clinical study of pegunigalsidase alfa, or PRX-102, for the treatment of Fabry disease. The head-to-head Phase III BALANCE clinical study is designed to evaluate the safety and efficacy of PRX-102 compared to agalsidase beta (Fabrazyme®) on renal function in Fabry patients with progressing kidney disease previously treated with agalsidase beta. BALANCE is the third of three Phase III studies, including the Phase III BRIDGE and the Phase III BRIGHT studies which are both fully enrolled and ongoing.

"We are excited to complete enrollment in our third Phase III study of PRX-102 for the treatment of Fabry disease. This achievement marks a major milestone in our development of PRX-102," said Dror Bashan, President and CEO of Protalix BioTherapeutics. "We are most grateful to the BALANCE study participants and to our investigators for their support and dedication, and we remain committed to bringing the Fabry community a potentially better treatment option. As we have already disclosed, we are targeting a BLA submission under an accelerated approval pathway for PRX-102 in the first quarter of 2020 based on data from our completed Phase I/II clinical studies of PRX-102 and from our ongoing Phase III BRIDGE clinical study. We believe our three, now fully enrolled, studies represent a robust clinical program for Fabry disease, and we look forward to reporting on the results upon completion of the studies."

PRX-102 is the Company's plant cell-expressed recombinant, PEGylated, cross-linked alpha-galactosidase A enzyme drug candidate. Protalix's products are recombinant therapeutic proteins expressed through its proprietary plant cell-based expression system, ProCellEx®.

"Despite years of current enzyme replacement treatment, there continues to be an unmet medical need in Fabry patients who continue to show progressive loss of renal function," said David G. Warnock, M.D., Professor of Medicine (Emeritus) at the University of Alabama at Birmingham. "The progressive loss of kidney function seen in Fabry patients may be the result of insufficient enzyme coverage combined with the presence of neutralizing antibodies. Given the favorable half-life of pegunigalsidase alfa and its low level of inhibition by pre-existing neutralizing antibodies, there is potential for pegunigalsidase alfa to attenuate and/or stabilize renal function in patients who continue to lose renal function while on currently-available enzyme replacement therapy."

About Protalix Biotherapeutics' Clinical Programs in Fabry Disease

The BALANCE Study is a 24-month, randomized, double blind, active control study of PRX-102 (pegunigalsidase alfa) in Fabry disease patients with impaired renal function. Patients previously treated with agalsidase beta for approximately one year and on a stable dose for at least six months were screened and then randomized to be switched and treated with 1 mg/kg of PRX-102 or continue treatment with 1mg/kg of agalsidase beta. Patients receive intravenous infusions of 1mg/kg administered every two weeks. Patients are randomized in a 2:1 ratio to PRX-102 or agalsidase beta. In the study, randomization is being stratified by urinary protein to creatinine ratio (UPCR) of < or ≥ 1 g/g by spot urine sample. No more than 50% of the patients enrolled in the study are female. Patients participating in the study are being evaluated to, among other disease parameters, determine if their renal function continues to deteriorate at the same rate while being treated with agalsidase beta as measured by eGFR slope. Cardiac assessment, Lyso-Gb3, pain, quality of life, immunogenicity, clinical events and pharmacokinetic and other parameters are also being evaluated. In addition, participating patients are being evaluated to assess the safety and tolerability of PRX-102.

The BRIDGE study is a 12-month open-label, single arm switch-over study to assess the safety and efficacy of pegunigalsidase alfa, 1 mg/kg infused every two weeks, in Fabry patients previously treated with agalsidase alpha (Replagal®). Enrollment in this study was completed in December 2018.

The BRIGHT study is a 12-month open-label switch-over study to assess the safety, efficacy and pharmacokinetics of pegunigalsidase alfa 2 mg/kg administered every 4 weeks in Fabry patients previously treated with an enzyme replacement therapy: agalsidase alfa or agalsidase beta. Enrollment in this study was completed in June 2019.

About Fabry Disease

Fabry disease is an X-linked inherited disease that results from deficient activity of the lysosomal enzyme alpha galactosidase A 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. Fabry patients inherit a deficiency of the enzyme alpha-galactosidase-A, 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)

The Company's proprietary pegunigalsidase alfa is an investigational, plant cell culture expressed enzyme, and a chemically modified version of, the recombinant alpha-Galactosidase-A protein. Protein sub-units are covalently bound via chemical cross-linking using short PEG chains, resulting in a more stable molecule with different pharmacokinetic parameters compared to the current available versions of the enzyme. In clinical studies, pegunigalsidase alfa has been observed to have a favorable circulatory half-life of approximately 80 hours. In addition, in a Fabry mouse model, pegunigalsidase alfa was observed to have favorable levels of enzyme activity in target organs affected by Fabry disease. The Company designed pegunigalsidase alfa to potentially address the continued unmet clinical need in Fabry patients of continuous disease progression, infusion reaction and immunogenicity.

About the Chiesi Group

Based in Parma, Italy, Chiesi Farmaceutici is an international research-oriented group with over 80 years' experience in the pharmaceutical sector and is present in 28 countries. The Group researches, develops and commercializes innovative medicines in respiratory disease, special care and rare disease therapeutic areas. The Group's Research & Development center is integrated with six other important research and development groups in France, the USA, the UK and Sweden, to promote its pre-clinical, clinical and registration programs. The Group employs around 5,700 people. Chiesi Group is a certified B Corp. For more 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®. Protalix was the first company to gain FDA approval of a protein produced through plant cell-based in suspension expression system. The Company's unique expression system represents a new method for developing recombinant proteins in a cost-effective, industrial-scale manner. Our pipeline consists of proprietary, potentially clinically superior versions of recombinant therapeutic proteins that target established pharmaceutical markets.

Protalix's first product manufactured by ProCellEx, taliglucerase alfa, was approved for marketing by the U.S. Food and Drug Administration (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 includes the following product candidates: pegunigalsidase alfa, a modified version of the recombinant human alpha-GAL-A protein for the treatment of Fabry disease, in Phase III clinical trials (BALANCE, BRIDGE and BRIGHT studies); and OPRX-106, an orally delivered anti-inflammatory treatment, and alidornase alfa for the treatment of Cystic Fibrosis, both in Phase II clinical trials. 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.

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," "plan," "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 our ability to identify and complete strategic alternatives on attractive terms or at all within the time period required to regain compliance with the continued listing standards of the NYSE American; risks related to our ability to continue as a going concern absent a refinancing or restructuring; risks related to any transactions we may effect in the public or private equity markets to raise capital to finance future activities; 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; risks related to our ability to continue as a going concern absent access to sources of capital we will need to finance future research and development activities, general and administrative expenses and working capital; risks related to any capital raising 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; slower than expected rates of patient recruitment; 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 lack of sufficient funding to finance clinical trials; the risk that the results of the clinical trials of our product candidates will not support our claims of superiority, 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 Chiesi Farmaceutici and any other collaborator, distributor or partner; risks related to the amount and sufficiency of our cash and cash equivalents; risks related to the ultimate purchase by Fundação Oswaldo Cruz of alfataliglicerase pursuant to the stated purchase intentions of the Brazilian Ministry of Health of the stated amounts, if at all; risks related to the successful conclusion of our negotiations with the Brazilian Ministry of Health regarding the purchase of alfataliglicerase generally; risks related to our commercialization efforts for alfataliglicerase in Brazil; risks relating to the compliance by Fundação Oswaldo Cruz with its purchase obligations and related milestones under our supply and technology transfer agreement; risks related to the amount and sufficiency of our cash and cash equivalents; risks related to the amount of our future revenues, operations and expenditures; the risk that despite the FDA's grant of fast track designation for pegunigalsidase alfa for the treatment of Fabry disease, we may not experience a faster development process, review or approval compared to applications considered for approval under conventional FDA procedures; risks related to the FDA's ability to withdraw the fast track designation at any time; 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; our ability to identify suitable product candidates and to complete preclinical studies of such product candidates; 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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