Protalix BioTherapeutics and Chiesi Farmaceutici Announce Successful pre-BLA Meeting with FDA for Accelerated Approval of pegunigalsidase alfa for the Treatment of Fabry Disease in the United States

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FDA indicated that existing clinical data, nonclinical data, safety database and manufacturing data will support a Biologics License Application submission

No additional clinical trials are necessary for BLA submission, expected by April of 2020

CARMIEL, Israel, Nov. 18, 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), today announced that they have completed a successful Type B Pre-Biologics License Application (BLA) meeting with the U.S. Food and Drug Administration (FDA) regarding the Accelerated Approval pathway for pegunigalsidase alfa (PRX-102) for the treatment of Fabry disease.

The Company, together with Chiesi, met with the FDA on October 15 to discuss key information on pegunigalsidase alfa to be included in a proposed BLA filing under the Accelerated Approval pathway. The Company and Chiesi report that they have reached alignment with the FDA on the Accelerated Approval pathway for pegunigalsidase alfa. The BLA, as expected to be submitted to the FDA, will include data from the Company's completed phase I/II clinical trials of pegunigalsidase alfa and from its ongoing phase III BRIDGE clinical trial.

"The confirmation by the FDA regarding the proposed BLA submission, together with the finalization of the BALANCE study enrollment (78 patients) and the very promising interim results from the BRIDGE study, are three recent significant consecutive milestones achieved with respect to our Fabry late-stage clinical program," said Dror Bashan, Protalix's President and Chief Executive Officer. "We are committed to the completion of this program with positive results for the benefit of the Fabry patient community."

The Company and Chiesi also announced that they have reached an agreement with the FDA regarding the ongoing BALANCE study, as currently designed, serving as the confirmatory trial for PRX-102. A confirmatory trial is required to convert a BLA approved under Accelerated Approval into a traditional approval.

The Company and Chiesi expect to submit the BLA to the FDA by April of 2020. The FDA indicated that the nonclinical data, the clinical data, the safety database and manufacturing data are sufficient to support the BLA submission, and that no additional clinical trials will be required for the proposed BLA submission. The Company and Chiesi expect that the fully electronic BLA submission will include a comprehensive set of preclinical, clinical and manufacturing related information on pegunigalsidase alfa. If approved, the Company will be eligible to receive a milestone payment from Chiesi.

"We have now had three successful interactions with the FDA during 2019, which built on our long-term relationship with the Agency and made our regulatory path forward for pegunigalsidase alfa clear," said Dr. Einat Almon, Protalix's Senior Vice President, Product Development. "We expect that alignment with the FDA on the Accelerated Approval pathway for pegunigalsidase alfa results in our being significantly closer to bringing an approved product to market to help Fabry patients. Together with our partner Chiesi, we look forward to completing the application process, as well as continuing with our double blind head-to-head phase III BALANCE clinical trial, which we feel will further strengthen the position of pegunigalsidase alfa within the Fabry patient community."

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, and chemically modified stabilized version of, the recombinant alpha-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, pegunigalsidase alfa has been observed to have a circulatory half-life of approximately 80 hours. The Company designed pegunigalsidase alfa to potentially address the continued unmet clinical need in Fabry patients of continuous disease progression, infusion reactions 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 a 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 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); OPRX-106, an orally delivered anti-inflammatory treatment, and alidornase alfa, 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 research and development activities, general and administrative expenses and working capital; 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; 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; and inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; 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 Chiesi Farmaceutici and any other collaborator, distributor or partner; 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 the amount of our future revenues 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; 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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