# Protalix BioTherapeutics Issues 2021 Letter to Stockholders

December 22, 2021

CARMIEL, Israel, Dec. 22, 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, today announced the following letter from its President and Chief Executive Officer, Dror Bashan, to its stockholders and the investment community.

Dear Protalix Stockholders,

As we look back and reflect on this past year, I am proud of our team and of the progress we have made in a time of continued Covid-19-related uncertainty across all corners of the globe. While the pandemic has added, and continues to add, many challenges that are out of our control, we remain resolute and focused on that which was within our control, including our operational, clinical and regulatory work. We continue to make progress on all fronts and firmly believe that we are on the right path forward towards meaningful, value-adding milestones and transformational catalysts.

I am pleased to briefly highlight some of our more notable milestones achieved in 2021.

***Regulatory Advancements***

Together with our development and commercialization partner, Chiesi Farmaceutici S.p.A., we completed a Type A meeting in October with the U.S. Food and Drug Administration (FDA) for the biologics license application (BLA) for PRX-102 for the treatment of adult patients with Fabry disease. We gained clarity regarding the FDA's expectations and confirmed our pathway for resubmission of a PRX-102 BLA, planned for the second half of 2022.

In addition, we have made important progress in our pre-submission activities toward an anticipated Marketing Authorization Application (MAA) with the European Medicines Agency (EMA). In our October meeting with the Rapporteur and Co-Rapporteur of the EMA, we and Chiesi discussed the MAA scope and gained general support for the anticipated PRX–102 MAA submission planned for the first quarter of 2022.

***Clinical Advancements***

The last patient in our Phase III *BALANCE* clinical trial, a 24-month, randomized, double blind, active control study of PRX-102 in Fabry patients with impaired renal function, received the final dose in October 2021. We anticipate releasing un-blinded final data in the second quarter of 2022 after all remaining patients have completed the 24-month treatment period. The determination to plan the PRX-102 MAA submission for the first quarter of 2022 was based on the interim analysis of the 12-month data generated from the *BALANCE* study, which were released in June 2021, in combination with previously reported positive data from our Phase III *BRIGHT* and *BRIDGE* clinical trials.

Earlier in the year, we announced positive topline results from our Phase III *BRIGHT* clinical trial, a 12-month, open-label, switch-over study designed to evaluate the safety, efficacy and pharmacokinetics of PRX–102 via intravenous (IV) infusions of 2 mg/kg administered every 4 weeks in Fabry patients previously treated with a commercially available enzyme replacement therapy (ERT). Topline results of the *BRIGHT* study indicate that 2 mg/kg of PRX-102 administered by IV infusion every 4 weeks are well tolerated among treated patients, and stable clinical presentation was maintained in adult Fabry patients.

***Corporate & Financial Developments***

Earlier this fall, we strengthened our balance sheet through exchanges of a substantial majority of our outstanding 7.50% Senior Secured Convertible Notes due 2021 for a combination of cash and new notes. In brief, we issued new 7.50% Senior Secured Convertible Notes due 2024 with an aggregate of $54.65 million principal amount and made principal and interest payments of approximately $27.00 million. The remaining 2021 Notes were repaid on the November 2021 maturity date. Over the course of the year, we raised almost $50.00 million in new equity, and we have an At-the-Market offering program in place should we find market conditions favorable for additional financing. These transactions secured our balance sheet, and we are gratified to be in a solid financial position to support our plans and strategies through our important, value-enhancing milestones.

***Looking Forward***

We have much to be thankful for this year, including our progress towards our BLA resubmission in the United States; important clarity on an MAA submission in Europe; positive data and progress across all of our clinical trials and a strengthened balance sheet. Going into the new year, we look forward with great anticipation to continuing our progress in advancing a potential good alternative for the Fabry community, and thank our employees

for their tireless efforts in driving Protalix forward and building on our scientific foundation. We also take this opportunity to express our appreciation for the close collaboration we have with Chiesi, our commercial partner. Finally, we would like to thank you, our stockholders, for your support and look forward to sharing our successes with you.

Sincerely,

Dror Bashan, President & Chief Executive Officer

**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.

**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 an updated BLA addressing the CRL for PRX–102; 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 PRX-102 will be commercially successful; the risk that the FDA, the EMA or other foreign regulatory authorities may not accept or approve a marketing application filed for PRX–102 or any of our other product candidates; 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; inability to monitor patients adequately during or after treatment; and or lack of sufficient funding to finance our clinical trials; the risk that the results of our clinical trials will not support the applicable claims of safety or efficacy and that our product candidates will not have the desired effects or will have undesirable side effects or other unexpected characteristics; risks relating to our ability to make required payments under our outstanding convertible notes or any other indebtedness as they come due and our ability to obtain additional financing and raise capital as necessary should the regulatory approval process become more extended; risks associated with the COVID-19 outbreak and variants, which may adversely impact our business, preclinical studies and clinical trials; risks relating to our evaluation and pursuit of strategic alternatives; risks relating to our ability to manage our relationship with our collaborators, distributors or partners; risks relating to changes to interim, topline or preliminary data from clinical trials that we announce or publish; 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; risk of significant lawsuits, including stockholder litigation, which is common in the life sciences sector; our dependence on performance by third-party providers of services and supplies; the impact of development of competing therapies and/or technologies by other companies; risks related to our supply of drug product to Pfizer; risks related to our expectations with respect to the potential commercial value of our product and product candidates; risks relating to the compliance by Fundação Oswaldo Cruz, an arm of the Brazilian Ministry of Health, with its purchase obligations under our supply and technology transfer agreement, which may have a material adverse effect on us and may also result in the termination of such agreement; potential product liability risks, and risks of securing adequate levels of related insurance coverage; the possibility of infringing a third-party's patents or other intellectual property rights and the uncertainty of obtaining patents covering our products and processes and successfully enforcing our intellectual property rights against third-parties; risks relating to changes in healthcare laws, rules and regulations in the United States or elsewhere; and the possible disruption of our operations due to terrorist activities and armed conflict, including as a result of the disruption of the operations of regulatory authorities, our subsidiaries, our manufacturing facilities and our customers, suppliers, distributors, collaborative partners, licensees and clinical trial sites; 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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