PROTALIX Biotherapeutics

PROTALIX BIOTHERAPEUTICS

CORPORATE PRESENTATION

September 2022

Note Regarding Forward-Looking Statements

This presentation (the “Presentation”) contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The forward-looking statements include, among others, statements related to: the timing and progress of the preparation of a Biologics License Application (BLA) resubmission addressing the complete response letter; risks related to the timing, progress and likelihood of final approval by the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) of a resubmitted BLA and of a Marketing Authorization Application, respectively, for PRX-102 and, if approved, whether the use of PRX-102 will be commercially successful; likelihood that the FDA, EMA or other applicable health regulatory authorities will approve an alternative dosing regimen; 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 to satisfactorily demonstrate non-inferiority to approved therapies; 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 our preparation and filing of, or in the approval or potential rejection of, any applications we file with the FDA, EMA or other health regulatory authorities for our other product candidates, 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; 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 the Company’s filings with the U.S. Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of today’s date. The Company undertakes no obligation to update or revise the information contained in this Presentation whether as a result of new information, future events or circumstances or otherwise.

Investment Highlights

Plant cell expressed recombinant proteins with improved therapeutic profiles

Revenue Generating, FDA-Approved Drug

FDA approved, commercially marketed drug for Gaucher disease. Elelyso® (alfataliglicerase in Latin America).

Clinically-Validated Platform

Proprietary ProCellEx® platform for recombinant protein expression cGMP manufacturing facility successfully inspected and audited by multiple regulatory agencies, including the FDA & EMA.

Fabry Disease Product Candidate

Completed three Phase 3 studies of PRX-102 for the treatment of Fabry Disease. Submitted a Marketing Authorization Application to the European Medicines Agency (EMA) in February 2022. Protalix and Chiesi Farmaceutici S.p.A. are preparing for a BLA resubmission to the U.S. FDA in 2H'22.

Pipeline

Uricase (PRX-115) for the treatment of severe gout,
LA DNase I (PRX-119) for the treatment of NETs-related diseases, as well as other product candidates, in discovery and preclinical phases.

Partnerships

Chiesi Farmaceutici S.p.A.
Pfizer Inc.
Fundação Oswaldo Cruz (Fiocruz)

Solid Balance Sheet

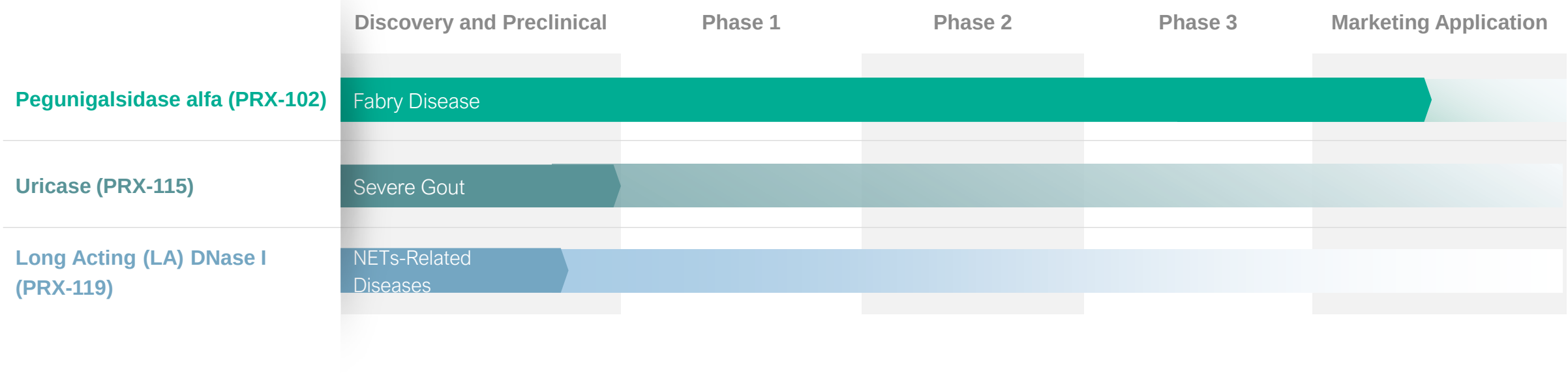
Successfully completed a Note Exchange in late 2021, which effectively extended the maturity of the 2021 Sr. Sec. Convertible Notes until 2024 and lowered the aggregate principal amount by approximately half.

PROTALIX Biotherapeutics

Note: cGMP = Current Good Manufacturing Practice.

Product Pipeline

Recombinant proteins designed to have potentially improved therapeutic profiles that target unmet medical needs and established pharmaceutical markets



All of our pipeline candidates are recombinant proteins expressed via our proprietary ProCellEx® system.

ProCellEx®: Protalix's Differentiated Plant Cell Protein Expression Platform

Unique Genetic Engineering Tools

Generates **improved tobacco plant cell lines** expressing plant unique expression cassettes designed to produce therapeutic proteins with **optimized pharmacokinetic and pharmacodynamic profiles**

Customized Chemical Modifications

Produces complex glycosylated proteins with potentially improved biologic attributes, including **reduced immunogenicity** and **enhanced protein stability/activity**

Intellectual Property Advantages

Proprietary manufacturing processes and development of 2nd generation products, related to Composition of Matter protection and FTO (Freedom-to-Operate)

Optimized for Complexity

Ability to express proteins that are difficult to express in other cell-based systems

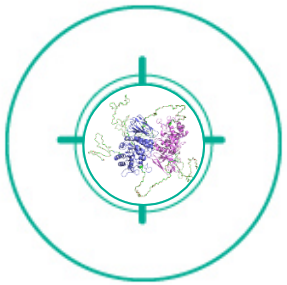
Streamlined Production Process

Simplified maintenance with **high batch-to-batch reproducibility** and **no risk of viral contamination**

Poised for Flexible Scale-Up

GMP-compliant infrastructure with modular capabilities allows for **rapid horizontal scale-up** to maintain production volume

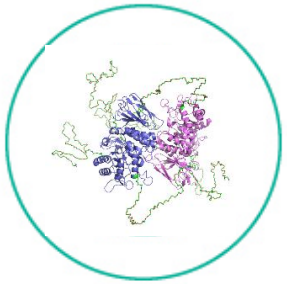
From Concept to Market



Selecting the target protein-drug candidate

Gene of interest engineering

Plant cells genetically engineered to express the gene of interest



Protein drug enhancement modifications

Improving biological dynamics to bring forth potentially improved clinical profiles

Pilot production with ProCellEx® platform

Purification and isolation

Product development

Clinical development and regulatory activity

Commercial production

Scaling up to produce commercial quantities

PROTALIX Biotherapeutics

Tekoah et al. Large-scale production of pharmaceutical proteins in plant cell culture-the Protalix experience. Plant Biotechnol J. 2015 (pp.1-10)

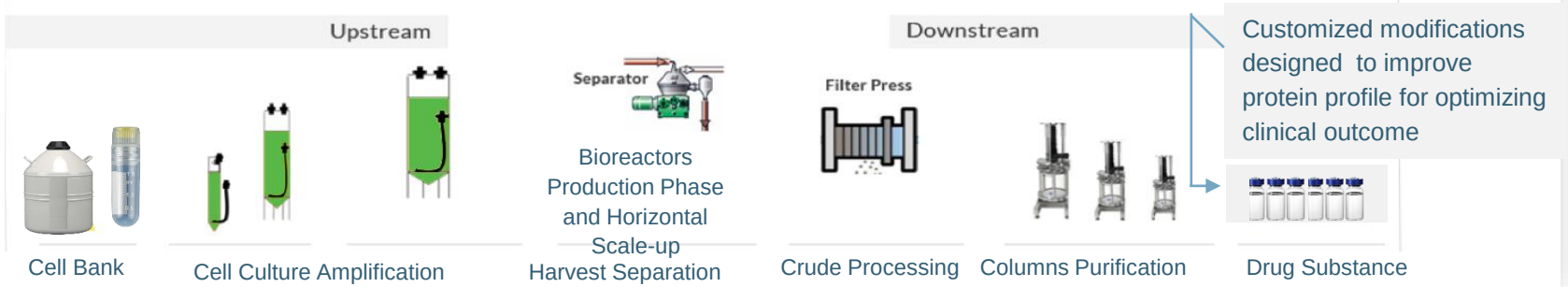
ProCellEx® Platform: Proprietary Protein Plant Cell Expression System

Unique capabilities of tailored genetic engineering and protein engineering tools for customized pre/post production modifications, with capacity for commercial scale-up

DEVELOPMENT OF TRANSGENIC CELL LINES FOR PRODUCTION OF TARGET PROTEIN

Agrobacterium mediated cell transformation using the natural capability of the agrobacteria to transfer DNA fragment into a plant chromosome

PROCESS OVERVIEW



ProCellEx® Plant Cell Production: Proven Advantages Over Other Cell-Based Production Technologies

Flexible polyethylene disposable bioreactors optimized for plant cell cultures

Large-Scale Plant Cell Production Advantages

- Rapid product roll-out and development
- No risk of viral contamination from mammalian components
- Manufacturing maintained at room temperature
- Highly tolerant of small changes in production conditions, including Ph and temperature
- Easy to use and maintain, with no requirement for complicated monitors
- Maintain production parameter constant → high reproducibility
- Independent, separately controlled, disposable bioreactors - no “cross talking”
- Rapid and flexible horizontal scale-up in accordance with changing production needs

Mammalian Cell Expression

Chinese Hamster Ovary (CHO) cell lines

- High set-up costs involving large bioreactors
- Cell cultures require a complex medium; small changes in composition may affect product characteristics
- Require highly controlled growth conditions in the bioreactor (e.g., Ph., temp and CO_2)
- Susceptibility to viral contaminations

Bacteria and Yeast Cell Expression

Bacteria or yeast cell lines

- Limited to non-glycosylated simple proteins
- Cannot produce antibodies, enzymes, and other complex proteins

Platform Validation: Elelyso® for Gaucher Disease

First plant cell derived recombinant protein approved by the FDA

Validation of the ProCellEx® platform

Gaucher disease is a rare genetic disorder characterized by the deposition of glucocerebroside in cells of the macrophage-monocyte system. Possible symptoms include enlarged liver and spleen, various bone disorders, easy bruising, and anemia. Left untreated, Gaucher disease can cause permanent body damage and decrease life expectancy.

Elelyso (alfataliglicerase) is approved in 23 markets[1]. Monetized through a world-wide exclusive license agreement with Pfizer in 2009, amended in 2015 (excluding Brazil).

Elelyso provides a consistent (and growing) revenue stream for Protalix while validating the ProCellEx platform technology and demonstrating the company's manufacturing and production expertise and ability to bring a treatment from concept to market production.

- Sales of ~$5.45 M in Brazil (YTD 2022)
- ~25% market share in Brazil
- ~10% annual growth expected over next 3 years

1. Approved in 23 markets including the US, Australia, Canada, Israel, Brazil, Russia and Turkey. The European Committee for Medicinal Products for Human Use (CHMP) gave a positive opinion but also concluded that the medicine cannot be granted marketing authorization in the EU because of the market exclusivity that had been granted to Vpriv® (Shire), which was authorized in August 2010, for the same condition. According to the EMA, this orphan market exclusivity is scheduled to expire on August 30, 2022.

Pegunigalsidase Alfa Has Significant Potential in Fabry Disease

Fabry Disease

X-linked lysosomal storage disorder caused by deficiency of lysosomal enzyme α–galactosidase-A

Occurs in one of every 40,000 people

Ultimately can result in end-organ failure, particularly of kidneys

Current standard of care is enzyme replacement therapy (ERT), which replaces the missing enzyme with a recombinant form of the protein via intravenous infusion every 2 weeks

Growing Market

~$2.1B+ growing market, despite limitations of current SOC

Expected CAGR ~10%

Potential 20-25% global market share

Will potentially be entitled to $150M-$200M royalties a year

~$2.1B

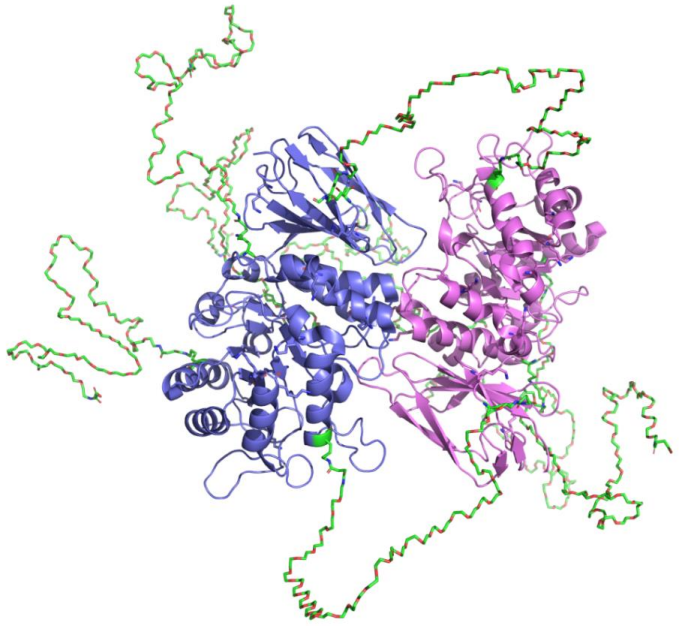
Global Market

Fabry Disease Competitive Landscape

Product Name	Fabrazyme®	Replagal®	Galafold®
Parent Company	Sanofi (Genzyme)	Takeda (Shire)	Amicus
Mechanism	ERT	ERT	Pharmacological chaperone
Indication	Fabrazyme (agalsidase beta) is indicated for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease. (U.S.) Fabrazyme is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α-galactosidase-A deficiency). Fabrazyme is indicated in adults, children and adolescents aged 8 years and older. (E.U.)	Replagal (agalsidase alpha) is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry Disease (α-galactosidase-A deficiency). (E.U.)	Galafold is an α-galactosidase-A pharmacological chaperone indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data. This indication is approved under accelerated approval based on reduction in kidney interstitial capillary cell KIC GL-3 substrate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. (U.S.) Galafold is indicated for long-term treatment of adults and adolescents aged 16 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase-A deficiency) and who have an amenable mutation (E.U.)
Approval Date	Full approval in 2021; accelerated approval in 2003 (U.S.); 2001 (E.U.)	Not approved in U.S.; 2001 (E.U.)	2018 (U.S.); 2016 (E.U.)
Treatment Type	Bi-weekly infusions	Bi-weekly infusions	Oral
Dosing	1 mg/kg every 2 weeks	0.2 mg/kg every 2 weeks	123 mg every other day

Pegunigalsidase Alfa: Chemically Modified, Plant Cell Derived, PEGylated, Covalently Bound Homodimer

- Pegunigalsidase alfa is a PEGylated enzyme designed to potentially have lower immunogenicity and an improved safety profile
- Covalent linked via short 2kD PEG having two reactive ends results in a more stabilized enzyme and extended circulatory and tissue half-life
- Continuous coverage/presence of enzyme over infusion intervals without compromising the enzyme activity and internalization to target organ and cells
- Providing potentially increased enzyme exposure and enhanced activity to target organs and sustain hydrolysis to prevent accumulation and re-accumulation of substrate
- PEGylation potentially reduces immunogenicity by masking immunogenic epitopes, which, together with the continued presence, has the potential to induce immune tolerance
- PEGylation potentially reduces the cross reactivity and reduces serum mediated enzyme inhibition of already existing antibodies (in patients previously treated with other ERT)
- Two optional dosing regimens based on unique product characteristics



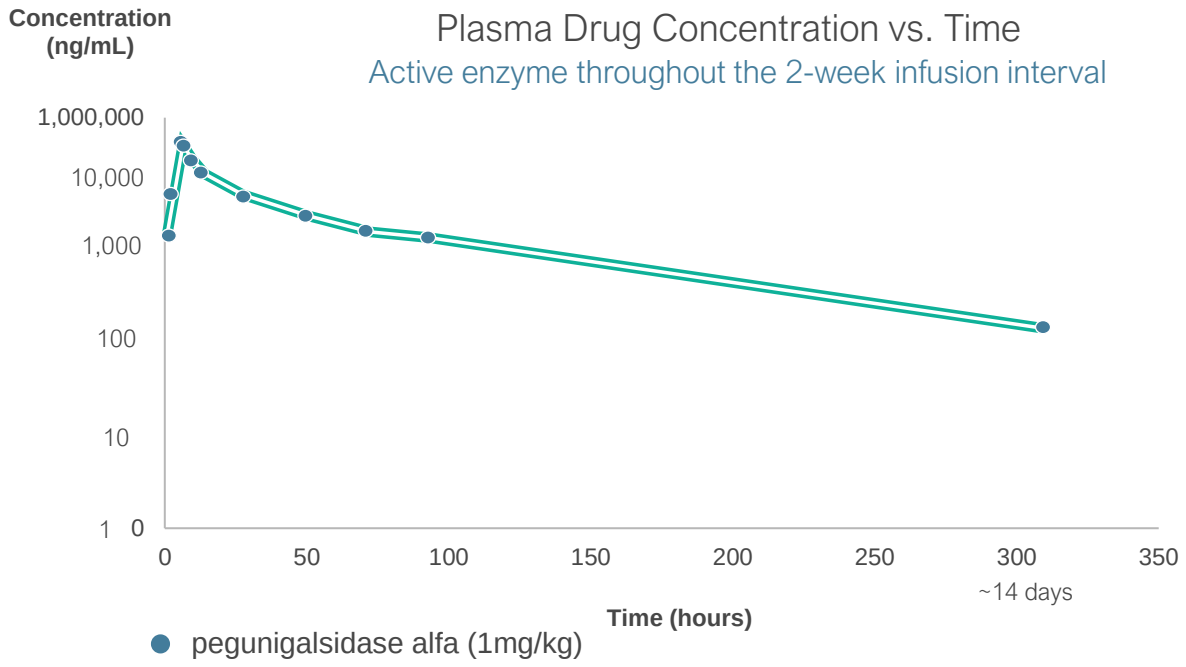
Ruderfer I., et al. Development and Analytical Characterization of Pegunigalsidase Alfa, a Chemically Cross-Linked Plant Recombinant Human α-Galactosidase-A for Treatment of Fabry Disease. Bioconjug Chem. 2018 (pp. 1-8)

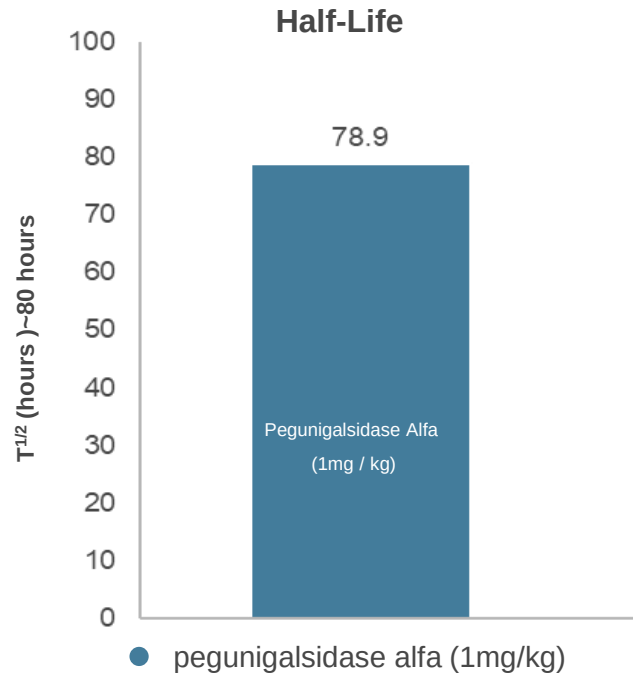
Schiffmann R., et al. Pegunigalsidase alfa, a novel PEGylated enzyme replacement therapy for Fabry disease, provides sustained plasma concentrations and favorable pharmacodynamics: A e 1/2 clinical trial. J of Inherited Metabolic Disease. 2019 (pp. 534-544)

Clinical Development Rationale Informed by Phase I/II Study

High levels of active available enzyme → potentially improved clinical benefit

Results of the Phase I/II Clinical Trial: Demonstrated stability throughout 2-week infusion interval





Pegunigalsidase Alfa: Robust Completed Clinical Development Program

Hundreds of patient years exposure to drug

	Phase I/II Study *n=18, 3+ 9 months*	Phase III BRIDGE Study *n=22, 12 months*	Phase III BRIGHT Study *n=30, 12 months*	Phase III BALANCE Study *n=78, 24 months*
Design / patients	Open-label, dose ranging study in **treatment-naïve** FD patients	**Open-label, switchover** study in FD patients previously treated with agalsidase alpha	**Open-label, switchover** study in FD patients previously treated with agalsidase beta or agalsidase alpha	**Head-to-head, randomized, active control, multicenter** in **treatment-experienced** (treated with agalsidase beta) FD patients • Randomized 2:1: pegunigalsidase alfa or agalsidase beta
Study drug(s) and dosage regimen	IV infusion of pegunigalsidase alfa • 0.2 mg/kg every 2 weeks • 1 mg/kg every 2 weeks • 2 mg/kg every 2 weeks *****_PB-102-F03: OLE study with 1 mg/kg up to 60 months_	IV infusion of pegunigalsidase alfa • 1 mg/kg every 2 weeks	IV infusion of pegunigalsidase alfa • 2 mg/kg every 4 weeks	IV infusion of pegunigalsidase alfa • 1 mg/kg every 2 weeks or IV infusion of agalsidase beta • 1 mg/kg every 2 weeks
Endpoints	**Primary:** Safety (number, severity and nature of AEs) **Secondary:** Kidney GB_3 via biopsies, Plasma Gb_3/lyso-Gb_3 levels, kidney function, cardiac fibrosis, cardiac ejection fraction, left ventricular mass index, immunogenicity	**Primary**: Safety (number, severity and nature of AEs) **Secondary:** Mean annualized change in eGFR, left ventricular mass index, plasma Gb_3/lyso-Gb_3 levels, quality of life	**Primary:** Safety (number, severity and nature of AEs) **Secondary:** Mean annualized change in eGFR, plasma Gb_3/lyso-Gb_3 levels, cardiac parameters, quality of life	**Primary:** Comparison of median annualized change in eGFR **Secondary:** Safety, Left ventricular mass index, plasma Gb_3/lyso-Gb_3 levels, quality of life
Status	**COMPLETE** ✓ Met Key Endpoints	**COMPLETE** ✓ Met Key Endpoints	**COMPLETE** ✓ Met Key Endpoints	**COMPLETE** ✓ Met Primary and Secondary Endpoints

All patients enrolled in studies have the opportunity to enter long-term, open label, extension studies investigating the long-term safety and efficacy of pegunigalsidase alfa

Summary of Clinical Activity Data from Phase 3 Trials

Phase 3 trials demonstrate clinical activity of Pegunigalsidase Alfa

bridge

Clinical trial population (n=22)

Substantial improvements in plasma lyso-Gb_3 levels were observed after 12 months of treatment in male patients and levels improved or remained stable throughout the study in female patients

- Mean overall annualized change in eGFR slope improved from -5.9 to -1.2 mL/min/1.73 m^2/year

bright

Clinical trial population (n=30)

Fabry disease progression, measured by eGFR slope and plasma lyso-Gb_3, was stable throughout pegunigalsidase alfa therapy

- Mean change of plasma lyso–Gb_3 of 3.01 nM from baseline (19.36 nM) to Week 52 (22.23 nM)
- Mean absolute change of eGFR from baseline of -1.27 mL/min/1.73/m^2/year

balance

Clinical trial population (n=78) randomized 2:1; PRX-102:agalsidase beta

The pre-specified non-inferiority margin was met and demonstrated that PRX-102 is statistically non-inferior to agalsidase beta

- The median (95% confidence interval) of the eGFR slope in the PRX-102 arm was -2.514 mL/min/1.73 m^2/year (-3.788, -1.240) and -2.155 mL/min/1.73 m^2/year (-3.805, -0.505) in the agalsidase beta arm

Summary of Safety Data from Phase 3 Trials

All trials to date show favorable tolerability and immunogenicity profiles

bridge

Patient population (n=22)

Favorable tolerability profile

Most TEAEs were mild or moderate in severity, with all AEs being transient

- 2 patients (9.1%) withdrew from treatment due to hypersensitivity reaction (resolved following withdrawal)

Favorable immunogenicity profile

bright

Patient population (n=30)

Favorable tolerability profile

No increase or relapse in pain reported

No de novo ADAs were reported following switch to PRX-102

Favorable immunogenicity profile

balance

Patient population (n=78)

Favorable tolerability profile

Less related TEAEs in PRX-102-treated patients (42 vs. 76 events or 42.85 vs. 152.91 adjusted to 100 treatment years)

Number of infusion-related reactions (IRR) adjusted to 100 infusions in the PRX-102 arm was 0.5 vs. 3.9 in the agalsidase beta arm

Favorable immunogenicity profile

Ongoing Extension Clinical Studies and Expanded Access

NCT03566017 — PB-102-F60: Open-Label Extension Study – 1 mg/kg Every Two Weeks

Phase I/II	10 completed	10 enrolled	97 enrolled (90 treated)
bridge	20 completed	18 enrolled	
balance	72 completed	69 enrolled	

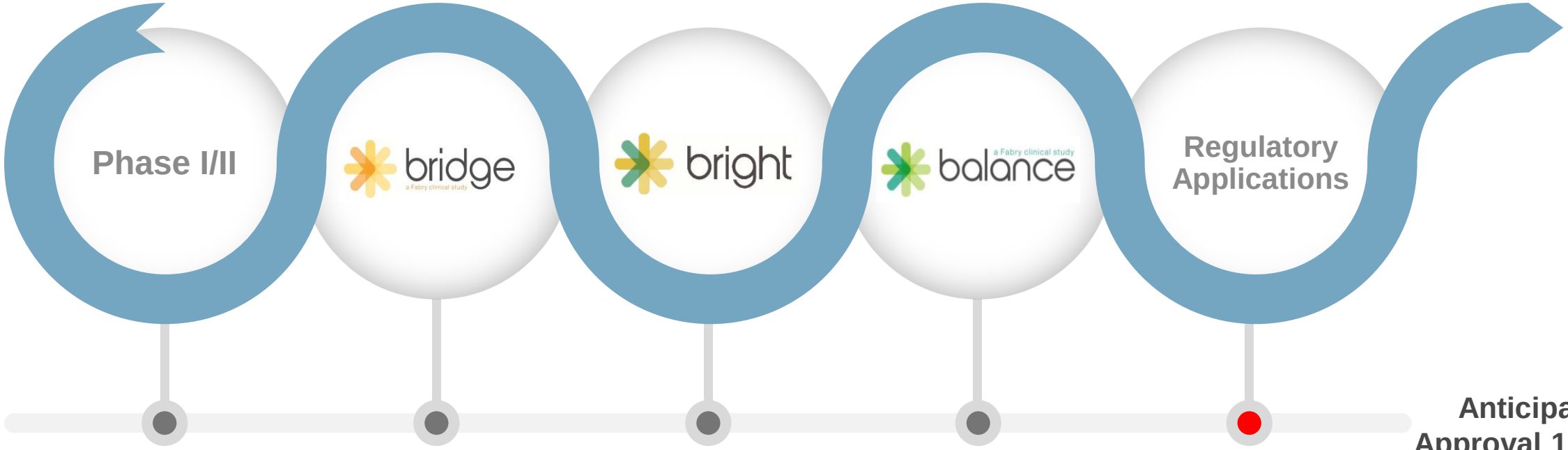
NCT03614234 — PB-102-F51: Open-label Extension Study – 2 mg/kg Every Four Weeks

bright	29 completed	29 enrolled	29 enrolled (28 treated)

NCT04552691 — Expanded Access Program in the US – Currently Enrolling

Robust Clinical Development Program Supports Regulatory Submissions

Hundreds of patient years exposure to drug



2018
Phase I/II
n=18
Met Key Endpoints ✓

2020
Phase III
n=22
Met Key Endpoints ✓

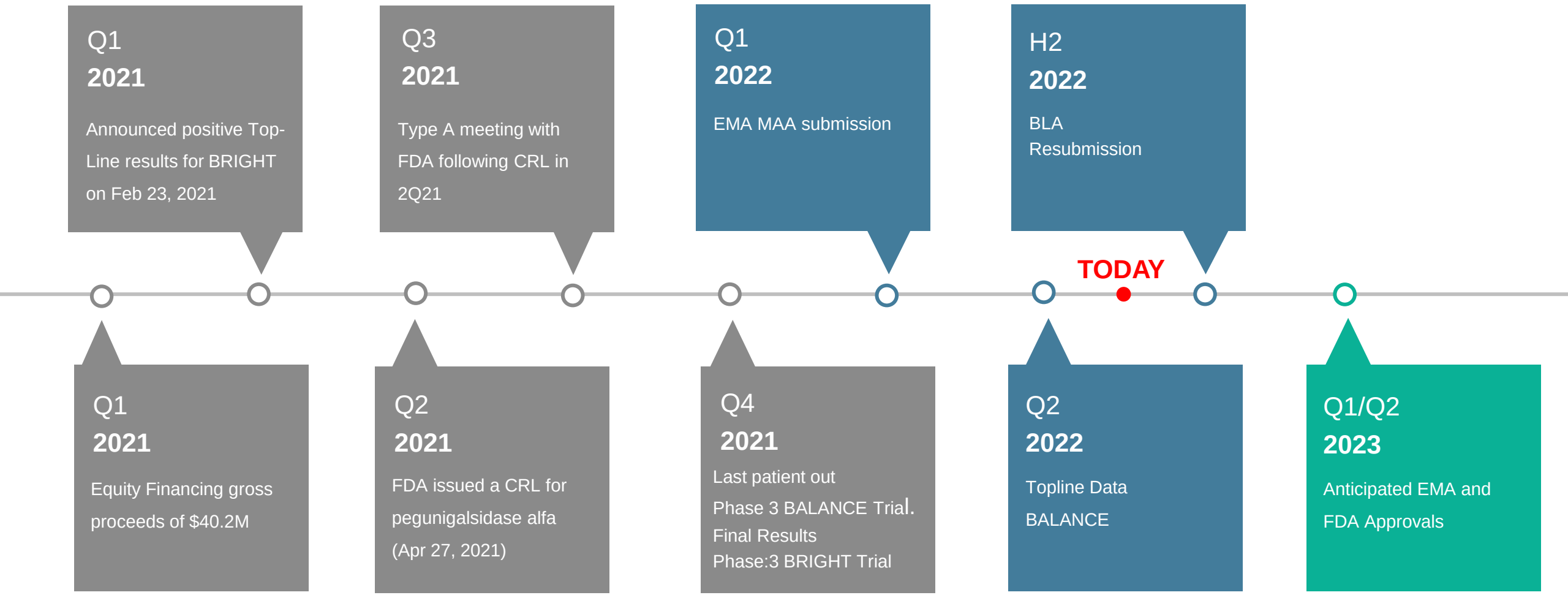
2021
Phase III
n=30
Met Key Endpoints ✓

2022
Phase III
n=78
Met Primary and Secondary Endpoints ✓

2022
Regulatory Submissions
European Medicines Agency MAA Submission ✓
U.S. FDA BLA Resubmission Planned 2H 2022

Anticipated Approval 1H 2023

Protalix Recent and Upcoming Expected Milestones



Committed Financial and Commercial Partner

Global Partnership with

Chiesi Farmaceutici S.p.A.

- International research-focused pharmaceuticals and healthcare group with ~$3B in revenue
- Operating in 30 countries with over 6,000 employees
- Talented Rare Disease Division with specific expertise in Fabry Disease
- Strong sales and marketing partner poised to maximize the market potential of pegunigalsidase alfa (pending approval) as the centerpiece of their new strategic U.S.-based Orphan Drug division

Up to $1+ billion in potential milestone payments

Tiered royalties of 15-35% (ex-US); 15-40% (US)

Committed global partner with a robust, expert sales team, the members of which have significant prior experience, and demonstrated expertise, in marketing ERTs

Growing Early Stage Pipeline

	Indication	Mechanism of Action	Status	Upcoming Milestones
Uricase (PRX-115)	Severe Gout	Recombinant uricase enzyme to lower uric acid levels	Preclinical studies show: Stable PK profile Long half-life Low immunogenicity High specific activity Toxicity study initiated (1Q'22)	Initiate Phase 1 study 1Q'23
Long Acting (LA) DNase I (PRX-119)	Neutrophil extracellular traps- (NET) related diseases	Recombinant DNase I to digest DNA-rich NETs and reduce NET toxicity	Preclinical studies show: Dose-dependent increase in survival in mouse model	

All of our pipeline candidates are recombinant proteins expressed via our proprietary ProCellEx® system.

Well Capitalized to Mature the Potential of PRX-102

CASH
$28.6 M (2Q'22)

REVENUE
$24.8 M in revenue (H1 2022)

FINANCING
Successfully completed a Note Exchange in 3Q'21 to effectively extend maturity from 2021 to 2024 and lower principal

NET BURN RATE
$5.7 M/Q

CASH RUNWAY
Cash Runway to 3Q'23

DEBT
$28.75 M in debt (Convertible Notes) due Sep. 2024

EQUITY OPPORTUNITIES
$20M At-the-Market Equity Facility w/HCW

SHAREHOLDER BASE
Strong Institutional stockholder base

UBS ALROV ROSALIND PSAGOT Since 1963 | The largest investment house in Israel HIR Investments MORE Investment House HIGHBRIDGE CAPITAL MANAGEMENT LLC

PROTALIX Biotherapeutics

Experienced Leadership Team

DROR BASHAN
President & CEO

Mr. Bashan has served as our President and Chief Executive Officer since June 2019. He has over 20 years of experience in the pharmaceutical industry with roles ranging from business development, marketing, sales and finance, providing him with both cross regional and cross discipline experience and a deep knowledge of the global pharmaceutical and health industries.

EINAT BRILL ALMON, PH.D.
Senior Advisor (former SVP, Chief Development Officer)

Dr. Almon joined Protalix in December 2004, with her latest role being Senior Vice President and Chief Development Officer. Since her recent retirement, she continues to serve us as a Senior Advisor, **with a facilitating role in the continued progress of our clinical development program.** She has many years of experience in the management of life science companies and projects including biotechnology and agrobiotech, with direct experience in clinical, regulatory, device and scientific software development, as well as a strong background and work experience in intellectual property.

EYAL RUBIN
SVP & CFO

Mr. Rubin has served as our SVP and Chief Financial Officer since September 2019. He brings to Protalix over 20 years of finance and capital markets experience, an extensive background in financial planning and operations, management and strategy and a deep knowledge of the biotechnology and pharmaceutical industries. Prior to Protalix, he served as EVP and CFO of BrainStorm Cell Therapeutics Inc., where he was responsible for corporate finance, accounting and investor relations activities.

YARON NAOS
SVP of Operations

Mr. Naos joined Protalix Ltd. in 2004 as a Senior Director for Operations and became our SVP, Operations. He has a wealth of hands-on experience and knowledge in the field of pharmaceutical development. Prior to Protalix, he served for a decade as R&D Product Manager at Dexxon Pharmaceutical Co., one of Israel's largest pharmaceutical companies, where he was responsible for technology transfer from R&D to production, and R&D activities that led to the commercialization of products.

YAEL HAYON, PH.D.
VP of R&D

Dr. Hayon brings to Protalix over a decade of experience in pharmaceutical research in development, both in the scientific operations and the administrative functions. She most recently served as VP of Clinical Affairs of Syqe Medical Ltd. Prior to her role at Syqe Medical, Dr. Hayon held positions at LogicBio Therapeutics, Inc. and Stem Cell Medicine Ltd. Dr. Hayon holds a Ph.D. in Neurobiology & Hematology, and an M.Sc. in Neurobiology, Hebrew University Faculty of Medicine, Israel.

Appendix

Uricase (PRX-115) for Severe Gout

PRX-115 is an investigational, PEGylated enzyme expressed via ProCellEx® for intravenous (IV) administration of recombinant Uricase being designed for the treatment of severe gout

Overview

- Gout is the most common form of chronic inflammatory disability, generally caused due to underexcretion of uric acid, leading to urate crystal deposition
- Severe gout[1] is a painful and severe form of inflammatory arthritis with frequent recurrent gout flares that can lead to, among other morbidities, bone grinding and joint deformities resulting in loss of function and disability; PRX-115 is being designed to treat patients with severe gout regardless of their treatment history
- Krystexxa® (Pegloticase), the only marketed recombinant Uricase for the treatment of refractory gout[2] (gout patients that have contraindication/failure of other lowering uric acid treatments), has a "Black Box" safety warning for anaphylaxis and infusion reactions, mediated by strong immunogenicity
- 89% of patients treated with Krystexxa® develop an immunogenic response that is associated with a failure to maintain normalization of serum uric acid levels over a 6-month therapy cycle[2]; a recent phase 4 study demonstrates that co-treatment with Pegloticase and methotrexate increases efficacy and tolerability in patients with uncontrolled gout[3]
- PRX-115 is being designed to lowering uric acid levels while having low immunogenicity and increase half-life in the circulation

Proprietary PEGylated Uricase

Pre-clinical data demonstrates:

- Stable PK profile and long half-life, low immunogenic risk, high specific activity

These preclinical data support the potential of PRX-115 to be a safe and effective treatment for severe gout.

- PRX-115 toxicity studies initiated in Q1'22
- PRX-115 development plan goal is to initiate Phase I clinical study in Q1'23

[1] Gout, Hyperuricaemia and Crystal-Associated Disease Network (G-CAN) consensus statement regarding labels and definitions of disease states of gout [Bursill D, et al. Ann Rheum Dis 2019;0:1–8]
[2] Efficacy and Tolerability of Pegloticase for the Treatment of Chronic Gout in Patients Refractory to Conventional Treatment [JAMA. 2011 Aug 17;306(7):711-20]
[3] Pegloticase in Combination With Methotrexate in Patients With Uncontrolled Gout: A Multicenter, Open-label Study (MIRROR); The Journal of Rheumatology 2021;48:767–74

Long Acting (LA) DNase I (PRX-119) for NETs-related diseases

PRX-119 is an investigational, cutting edge PEGylated recombinant human DNase I, expressed via ProCellEx®, designed to elongate DNase half-life in the circulation for the treatment of NETs-related diseases.

Overview

- Neutrophil extracellular traps (NETs) are web-like structures, released by activated neutrophils that trap and kill a variety of microorganisms. NETs are composed of DNA, histones, antimicrobial and pro-inflammatory proteins
- Excessive formation or ineffective clearance of NETs can cause different pathological effects. NETs formation was observed in various autoimmune, inflammatory and fibrotic conditions, diverse forms of thrombosis, cancer and metastasis[1]
- Animal studies demonstrated that DNase treatment reduces NETs toxicity[1]
- The only FDA approved DNase I, Dornase alfa (Pulmozyme®, Roche), is for the treatment of cystic fibrosis (CF) patients via inhalation. However, this enzyme has demonstrated relatively short half-life in the circulation[2] and may not be effective in treating other NETs-related diseases
- PRX-119 designed to elongate DNase half-life in the circulation for the treatment of acute and chronic conditions related to NETs

Proprietary PEGylated DNase:

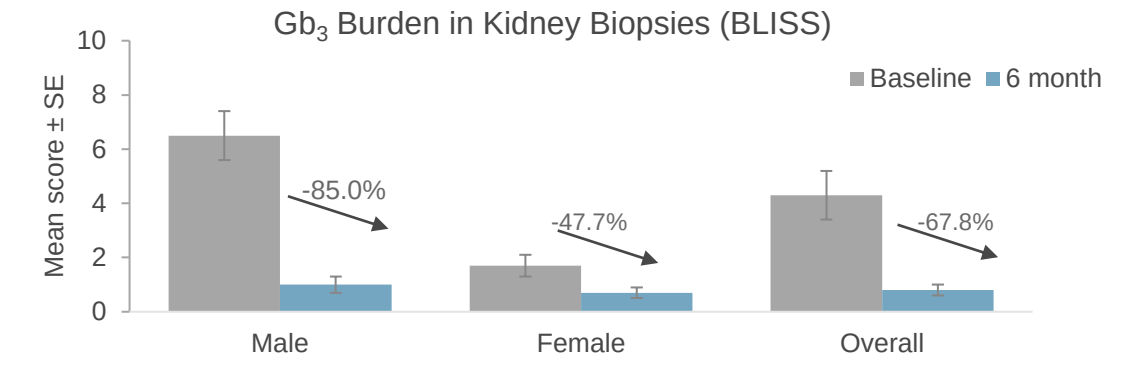
- Protalix is developing LA DNase I potentially to customize the treatment for various medical conditions in which NETs are involved
- In a Cecal Ligation and Puncture (CLP) mice sepsis model, the treatment of LA-DNase improved mice survival in a dose dependent manner, and with a greater effect than the unmodified DNase
- LA-DNase is being tested in mice sepsis model in one of the leading centers of the National Preclinical Sepsis Platform (NPSP) in Canada. This center has experience in accelerating the translation science of new therapies for clinical trials

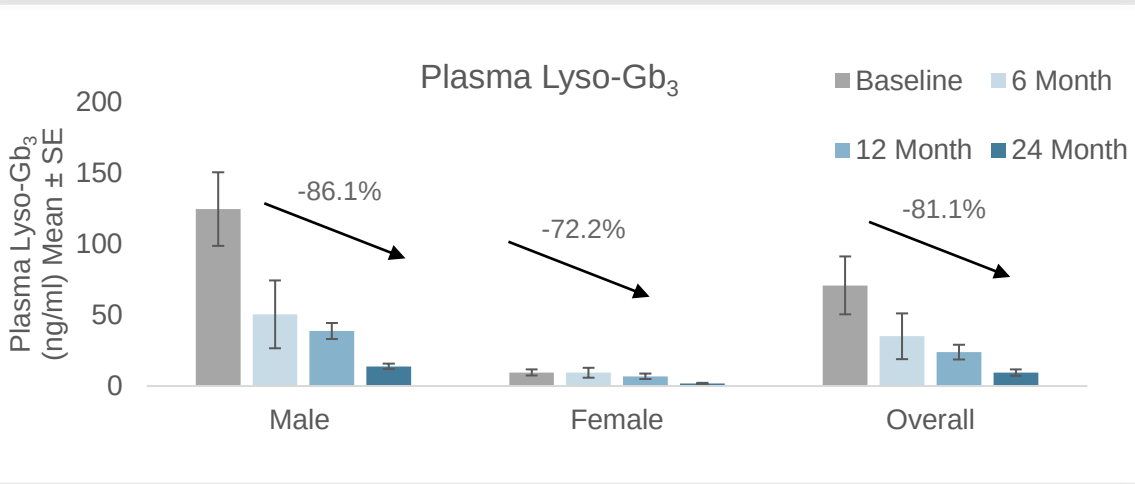
PROTALIX Biotherapeutics

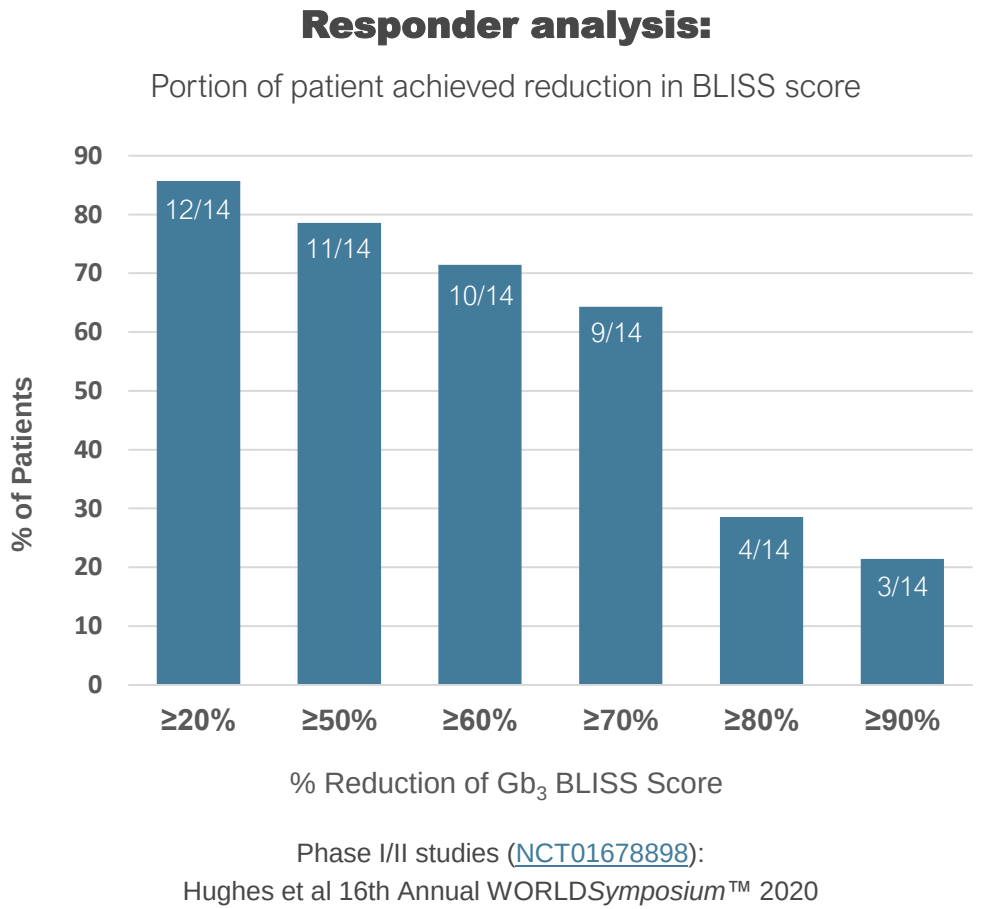
[1] Neutrophil extracellular traps in immunity and disease. Papayannopoulos V. Nat Rev Immunol. 2018 Feb;18(2):134-147
[2] Pharmaco-toxicological expert report Pulmozyme rhDNase Genentech, Inc. Green J D. Hum Exp Toxicol. 1994 May;13 Suppl 1:S1-42

Phase I/II Study

Substantial reduction & high correlation between two Fabry disease biomarkers: Gb_3 and Lyso-Gb_3







Phase I/II studies (NCT01678898):
Hughes et al 16th Annual WORLD*Symposium*™ 2020

BRIDGE Phase 3 Trial Summary

Demonstrated favorable tolerability, immunogenicity and clinical activity profiles

Safety Data

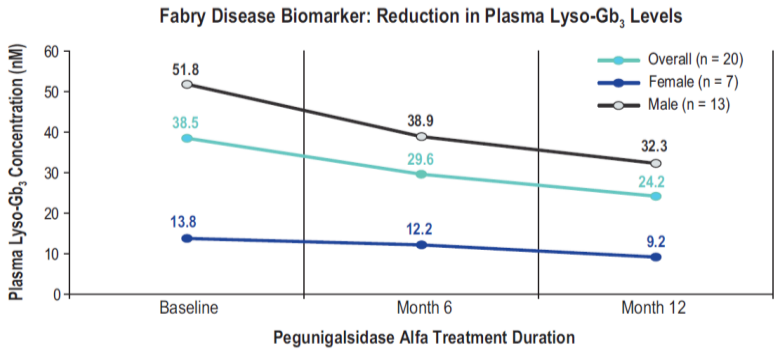
Favorable tolerability and immunogenicity profile

Most TEAEs were mild or moderate in severity, with all AEs being transient

2 patients (9.1%) withdrew from treatment due to hypersensitivity reaction (resolved following withdrawal)

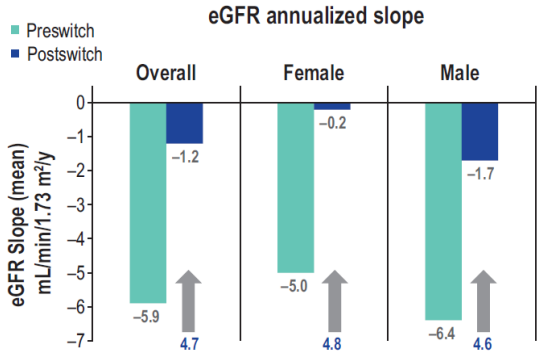
Only patients (n=2) with pre-existing ADAs were positive for neutralizing antibodies

Efficacy Data



Lyso-Gb_3, plasma globotriaosylsphingosine.

Overall, mean plasma lyso-Gb_3 concentrations decreased by 31.5% from a baseline of 38.5 nM to 24.2 nM with treatment at month 12



eGFR, estimated glomerular filtration rate.

Mean overall annualized eGFR slope improved from -5.9 to -1.2 mL/min/1.73 m^2/year

BRIGHT Phase 3 Trial Summary

Demonstrated favorable tolerability, immunogenicity and clinical activity profiles

Safety Data

Favorable tolerability profile

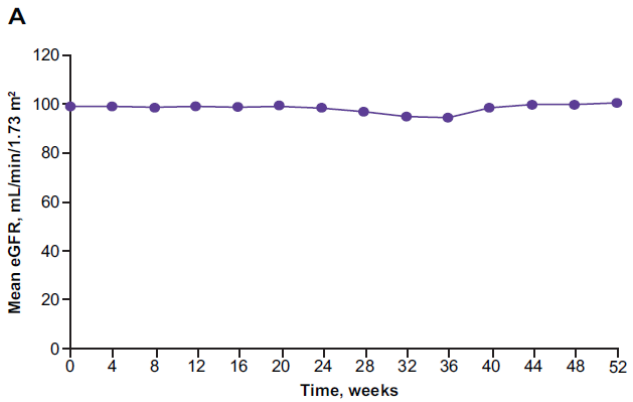
Reduction of infusion duration, indicating good drug tolerability

No increase or relapse in pain reported

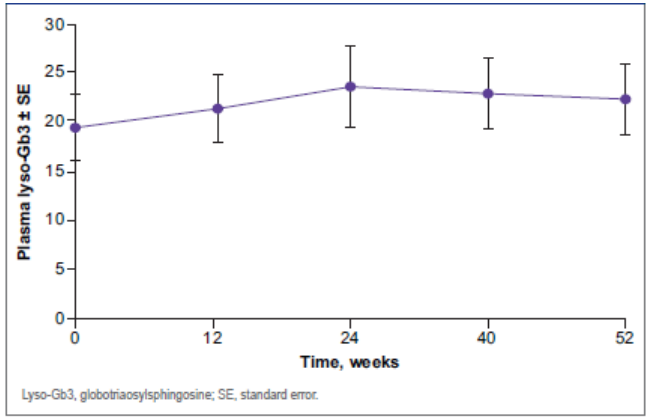
No de novo ADAs were reported following switch to PRX-102

Efficacy Data

Stable Fabry disease progression, measured by eGFR slope and plasma lyso-Gb_3, throughout pegunigalsidase alfa therapy



Mean absolute change of eGFR from baseline of –1.27 mL/min/1.73 m^2



Mean change of plasma lyso–Gb_3 of 3.01 nM from baseline (19.36 nM) to Week 52 (22.23 nM)

BALANCE Phase 3 Trial Summary

Demonstrated favorable tolerability, immunogenicity and activity profiles

Safety Data

Favorable tolerability and immunogenicity profile

Less related TEAEs in PRX-102-treated patients (42 vs. 76 events or 42.85 vs 152.91 adjusted to 100 treatment years)

Number of infusion-related reactions adjusted to 100 infusions in the PRX-102 arm was 0.5 vs. 3.9 in the agalsidase beta arm

Efficacy Data

The pre-specified non-inferiority margin was met and demonstrated that PRX-102 is statistically non-inferior to agalsidase beta

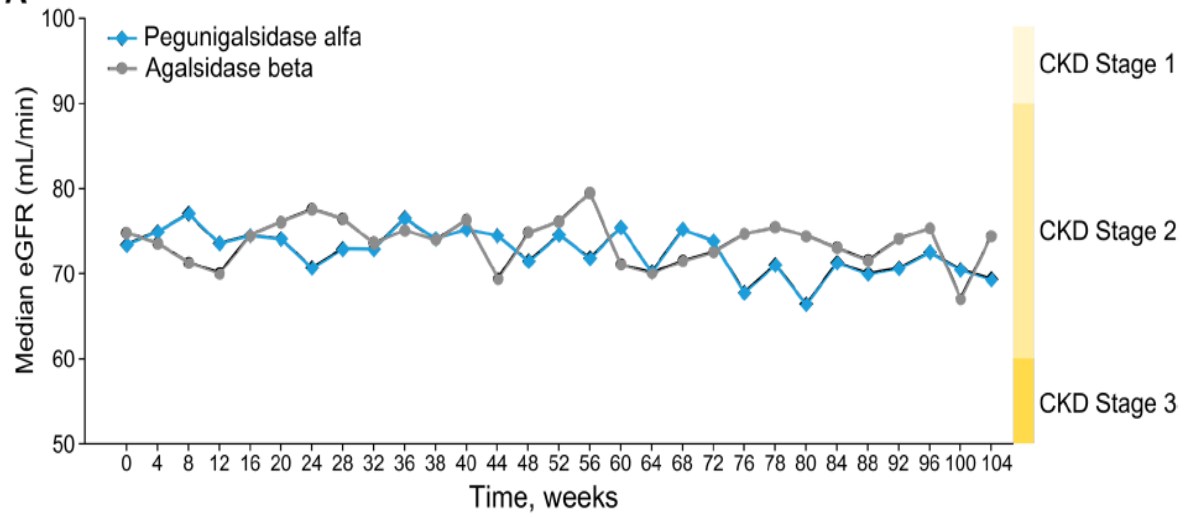
ITT*– Primary Analysis	PRX-102 (N=52)	Agalsidase Beta (N=25)
eGFR slope - Adjusted median	-2.514	-2.155
95% CI for the median	-3.788; -1.240	-3.805; -0.505
Median difference (95% CI for the difference in medians)	-0.359 (**-2.444**; 1.726)	

*The Intent to Treat (ITT) population - all randomized patients who received at least one dose (including partial dose) of the study medication (PRX-102 or agalsidase beta)

BALANCE Study – Primary Efficacy Analysis

Evaluation of Renal Function (A) median eGFR values over time (B) primary efficacy analysis of the median difference in eGFR slope between baseline and 24 months

A



B eGFR median slope analysis ($eGFR_{CKD\ EPI}$), mL/min/1.73 m^2/year

	Pegunigalsidase alfa n = 52	Agalsidase beta n = 25	Difference[a]
Median	−2.514	−2.155	−0.359
95% Confidence interval	(−3.788, −1.240)	(−3.805, −0.505)	(−2.444[b], 1.726)

[a](Pegunigalsidase alfa) - (agalsidase beta).
[b]Value above the predefined noninferiority margin.
CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; $eGFR_{CKD-EPI}$, eGFR chronic kidney disease-epidemiology collaboration equation.

BALANCE Study Results

Treatment Emergent Adverse Events

	Pegunigalsidase alfa n=52	Agalsidase beta n=25	Overall N=77
Any TEAE			
Events, n (rate[a])	561 (572)	406 (817)	967 (655)
Patients, n (%)	47 (90%)	24 (96%)	71 (92%)
Related TEAEs			
Events, n (rate[a])	42 (43)	76 (153)	118 (80)
Patients, n (%)	21 (40%)	11 (44%)	32 (42%)
Related Serious TEAEs			
Events, n (rate[a])	1 (1)	0	1 (0.7)
Patients, n (%)	1 (2%)	0	1 (1%)
Related TEAEs Leading to Withdrawal			
Events, n (rate[a])	1 (1)	0	1 (0.7)
Patients, n (%)	1 (2%)	0	1 (1%)
IRRs			
Events, n (rate[b])	13 (0.5)	51 (3.9)	64
Patients, n (%)	11 (21%)	6 (24%)	17 (22%)

[a] Per 100 exposure-years.
[b] Per 100 infusions.
IRR, infusion-related reaction; TEAE, treatment-emergent adverse events.

Conclusions:

- Pegunigalsidase alfa showed noninferiority to agalsidase beta based on the median eGFR annualized slope, a key measure of FD progression
- No new safety concerns were identified
  – Overall, the tolerability and immunogenicity profiles were favorable for patients who switched to pegunigalsidase alfa
    - The rate of related TEAEs was approximately 4-fold lower for pegunigalsidase alfa than for agalsidase beta
    - The proportion of ADA+ patients with nAbs was lower for pegunigalsidase alfa than for agalsidase beta at 24 months
    - The event rate of IRRs was approximately 8-fold lower for pegunigalsidase alfa than agalsidase beta
- After study completion, most patients opted to continue treatment with pegunigalsidase alfa in an open-label extension study for 60 months (NCT03566017)