

PROTALIX BIOTHERAPEUTICS

C O R P O R A T E P R E S E N T A T I O N

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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. Forward-looking statements are subject to many risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements as a result of several factors. Examples of the risks and uncertainties include, but are not limited to, the following: that the U.S. Food and Drug Administration (FDA) might not grant marketing approval for PRX-102 by the PDUFA date or at all and, if approved, whether PRX-102 will have significant limitations on its use; risks related to the timing, progress and likelihood of final approval by the FDA and European Medicines Agency (EMA) of the resubmitted Biologics License Application and of a Marketing Authorization Application, respectively; risks related to the commercial success of PRX-102, and of our other product and product candidates, if approved; 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 reforms in the healthcare industry and the risk that uncertainty associated with pharmaceutical pricing, reimbursement and related matters could adversely affect the marketing, pricing and demand for our products, if approved; 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 and short-term bank deposits; 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 III studies of PRX-102 for the treatment of Fabry Disease. Submitted a Marketing Authorization Application to the European Medicines Agency (EMA) in February 2022. Resubmitted a BLA to the U.S. FDA in November 2022. PDUFA date is May 9, 2023.



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)



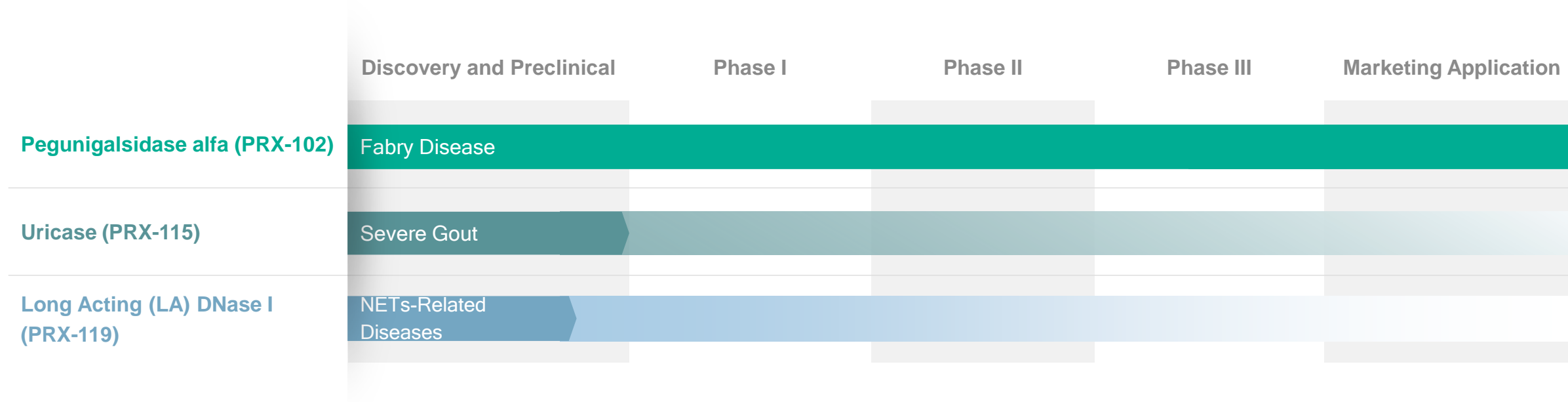
Solid Balance Sheet

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.



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 Protein Plant Cell 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

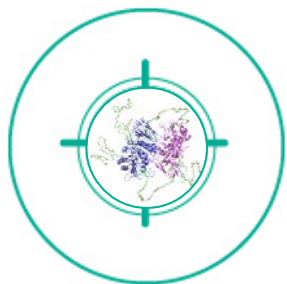
Streamlined Production Process

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

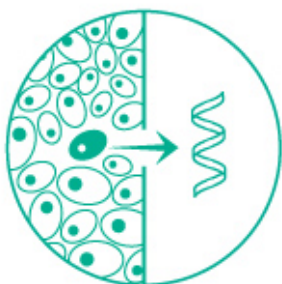
Poised for Flexible Scale-Up

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

From Concept to Market

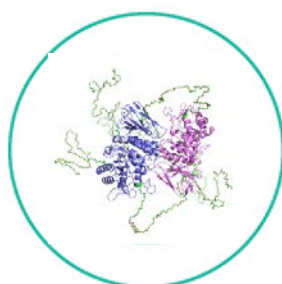


Selecting the
target protein-
drug candidate



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

ProCellEx[®] Platform: Proprietary Protein Plant Cell Expression System

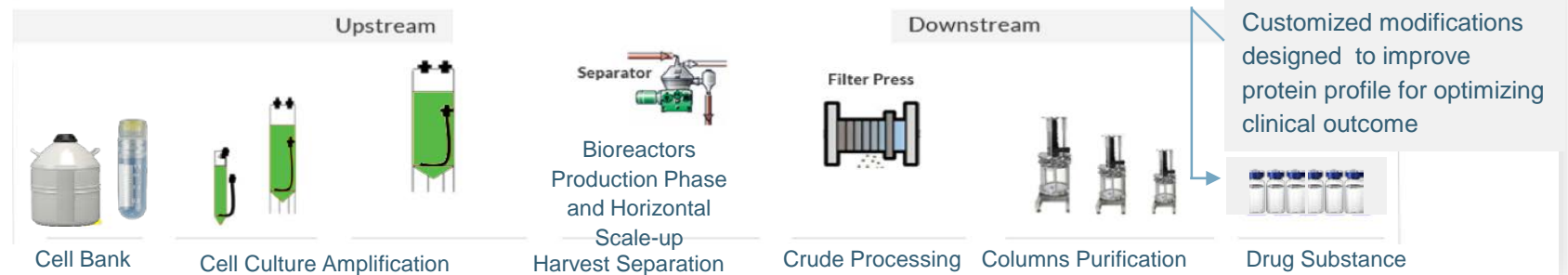
Unique capabilities of tailored genetic engineering and protein engineering tools for customized pre/post production modifications, with capacity for commercial scale-up

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 CO₂)
- 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

Gaucher Disease

ProCellEx[®] platform validation in lysosomal storage disorder



Rare autosomal recessive disorder

Occurs in approximately 1 in 40,000 live births

One of the most prevalent lysosomal storage disorders (LSD) in the world



Glucocerebrosidase (GCD) enzyme deficiency

Leads to accumulation of glucosylceramide, a lipid, in bone marrow, lungs, spleen, liver, and sometimes brain



Gaucher disease Type 1 Symptoms

Possible symptoms include enlarged liver and spleen, various bone disorders, easy bruising and bleeding and anemia

Left untreated, Gaucher disease can cause permanent body damage and decreased life expectancy



Standard of care is enzyme replacement therapy (ERT)

Patients are injected with recombinant GCD to replace the mutated or deficient natural GCD enzyme

Platform Validation: Elelyso® for Gaucher Disease

First plant cell derived recombinant protein approved by the FDA



Validation of the ProCellEx® platform

Elelyso (alfataliglycerase in Latin America) is a proprietary, recombinant form of GCD for long-term treatment of patients with a confirmed diagnosis of type 1 Gaucher disease

First plant cell-based recombinant therapeutic protein approved by the FDA or any other major regulatory authority

Approved in 23 markets¹

Monetized through a worldwide 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 ~\$7.2 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. In 2010, 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. The orphan market exclusivity expired in August 2022.

Fabry Disease



Rare X-linked recessive disease

LSD occurring in approximately 1 in 40,000 people worldwide

More prevalent in males than females



α -galactosidase-A enzyme deficiency

Leads to accumulation of the fatty substance globotriaosylceramide (Gb_3) in blood and blood vessel walls throughout the body

Causes channels of blood vessels to narrow, leading to decreased blood flow and tissue nourishment



Multisystemic Disease

Progressive disease that can lead to renal failure, cardiomyopathy with potentially malignant cardiac arrhythmias, and strokes

Symptoms such as abdominal and neuropathic pain can appear in patients as young as two years old



Standard of care is ERT

Patients are injected with recombinant α -galactosidase-A to replace the deficient enzyme

Two ERTs are available in various countries: agalsidase alfa (Replagal[®]) or agalsidase beta (Fabrazyme[®])^{1,2}

Pegunigalsidase Alfa Has Significant Potential in Fabry Disease

Prevalence:
1 in 40,000



Patients typically require regular, long-term treatment regimen to replace deficient enzyme

Patients who develop anti-drug antibodies or experience infusion-related reactions to current ERT could benefit from an alternative therapeutic option

\$2.1B+
Global Market



Expected growth at CAGR of approximately ~10% from 2020-2027

Potential 20-25% global market share

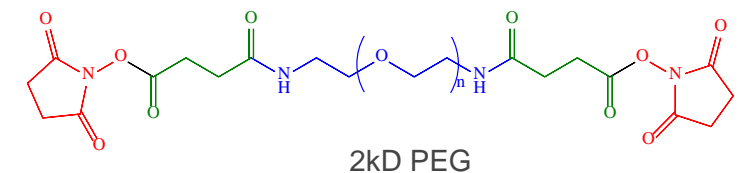
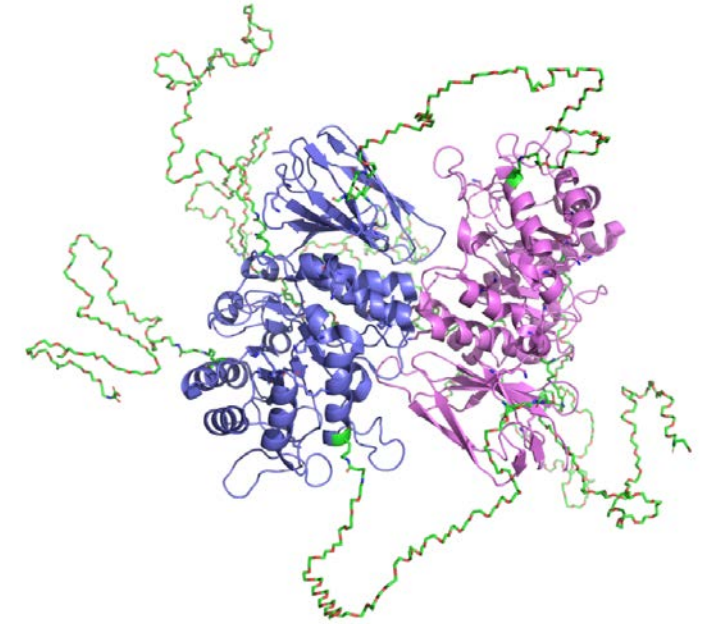
Will potentially be entitled to \$150M-\$200M royalties per year

Fabry Disease Competitive Landscape

Product Name	Fabrazyme®	Replagal®	Galafold®
Parent Company	Sanofi (Genzyme)	Takeda (Shire)	Amicus
Mechanism	ERT	ERT	Pharmacological chaperone
Indication	<p>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.)</p> <p>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.)</p>	<p>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.)</p>	<p>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.</p> <p>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.)</p> <p>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.)</p>
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 Linked Homodimer

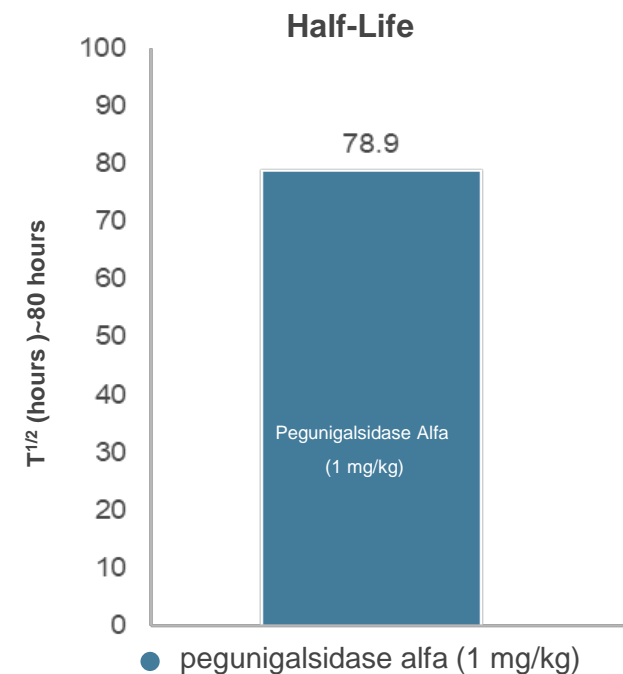
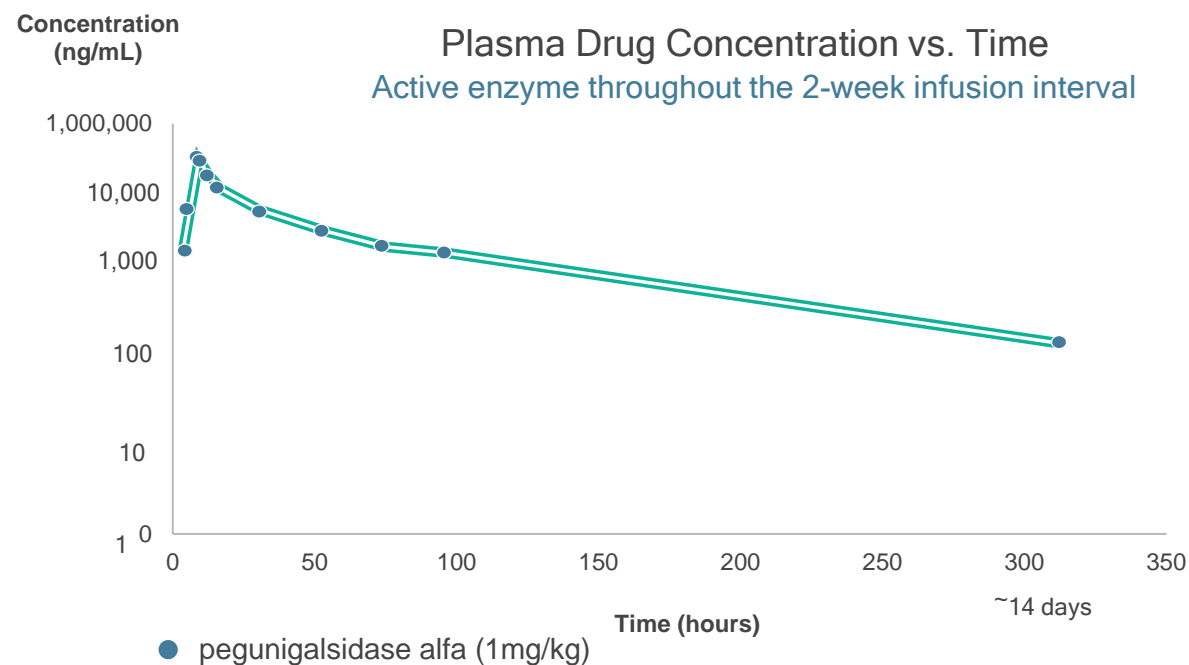
- Pegunigalsidase alfa is a PEGylated enzyme designed to potentially have lower immunogenicity and an improved safety profile
- Covalent linked via short 2kD PEG having two reactive ends results in a more stabilized enzyme and extended circulatory and tissue half-life
- Continuous coverage/presence of 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)
- Development of two alternative dose and regimens with potential for once every 4 weeks dosing



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 the treatment

	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 <ul style="list-style-type: none"> Randomized 2:1: pegunigalsidase alfa or agalsidase beta
Study drug(s) and dosage regimen	IV infusion of pegunigalsidase alfa <ul style="list-style-type: none"> 0.2 mg/kg every 2 weeks 1 mg/kg every 2 weeks 2 mg/kg every 2 weeks <i>*PB-102-F03: OLE study with 1 mg/kg up to 60 months</i>	IV infusion of pegunigalsidase alfa <ul style="list-style-type: none"> 1 mg/kg every 2 weeks 	IV infusion of pegunigalsidase alfa <ul style="list-style-type: none"> 2 mg/kg every 4 weeks 	IV infusion of pegunigalsidase alfa <ul style="list-style-type: none"> 1 mg/kg every 2 weeks or IV infusion of agalsidase beta <ul style="list-style-type: none"> 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 III Clinical Program

Program demonstrates clinical activity of pegunigalsidase alfa



Clinical trial population (n=22)

Substantial improvements in plasma lyso-Gb₃ 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 m²/year



Clinical trial population (n=30)

Fabry disease progression, measured by eGFR slope and plasma lyso-Gb₃, was stable throughout pegunigalsidase alfa therapy

- Mean change of plasma lyso-Gb₃ 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 m²/year



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 m²/year (-3.788, -1.240) and -2.155 mL/min/1.73 m²/year (-3.805, -0.505) in the agalsidase beta arm

Summary of Safety Data from Phase III Clinical Program

All trials to date show favorable tolerability and immunogenicity profiles



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



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



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)

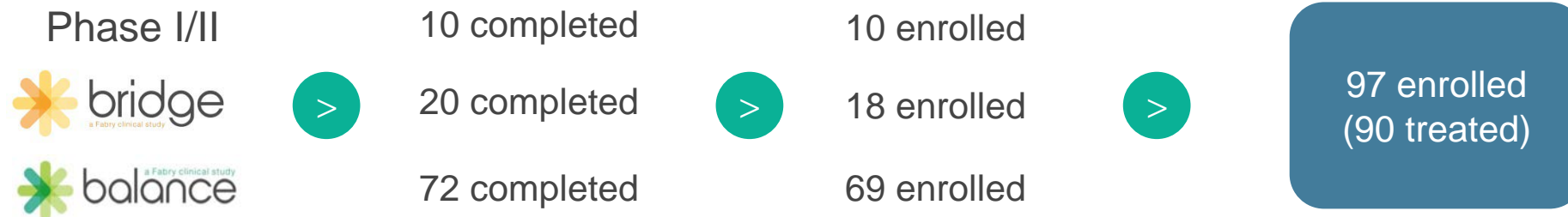
Number of infusion-related reactions (IRR) adjusted to 100 infusions in the PRX-102 arm was 0.5 vs. 3.9 in the agalsidase beta arm

Favorable immunogenicity profile

Ongoing Extension Clinical Studies and Expanded Access

NCT03566017

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



NCT03614234

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



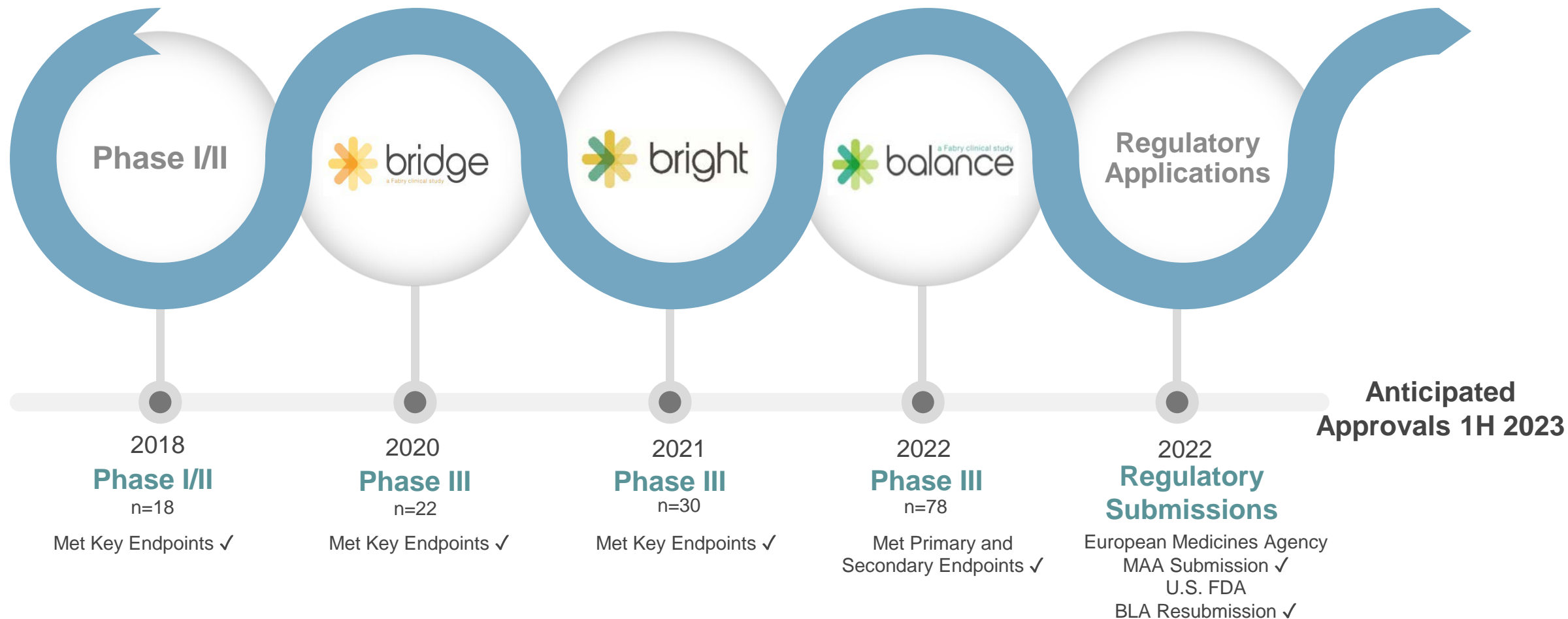
NCT04552691

Expanded Access Program in the US – Currently Enrolling

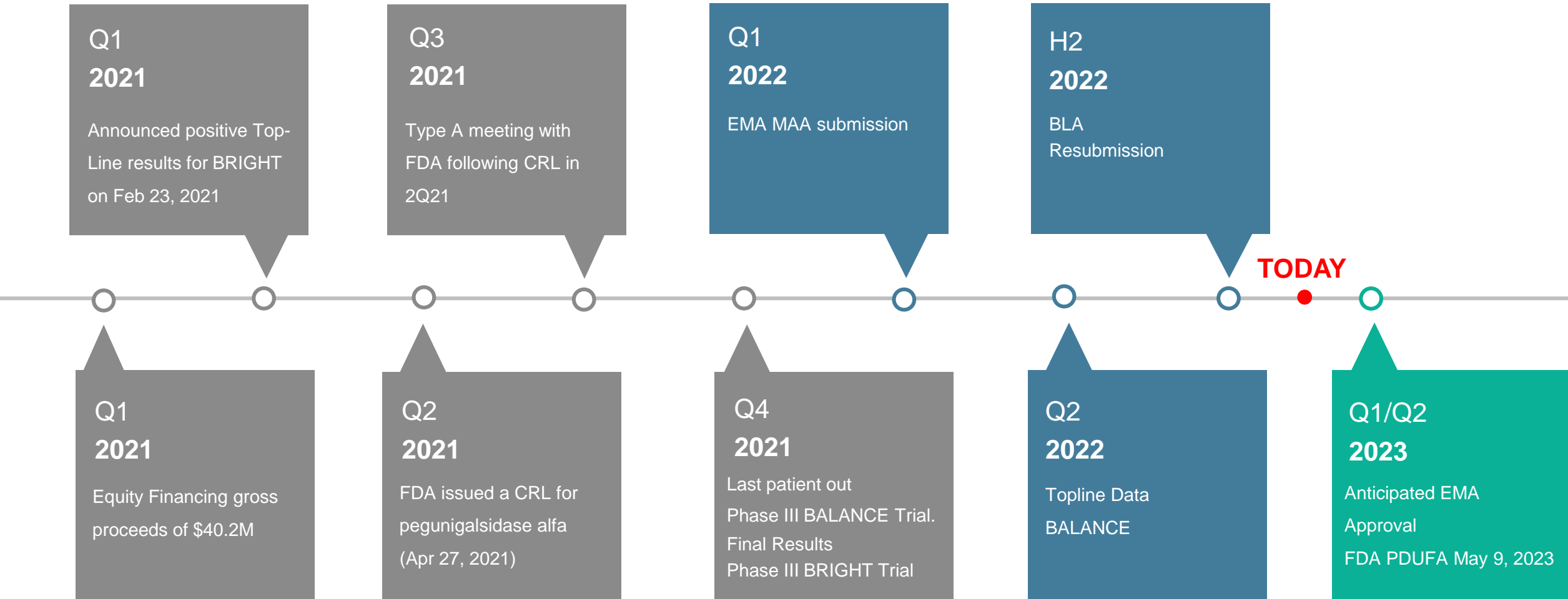
Robust Clinical Development Program Supports Regulatory Submissions

Worldwide, multicenter, program

Collaboration with TOP Fabry disease KOLs and patient groups



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 I study 1Q'23
Long Acting (LA) DNase I (PRX-119)	Neutrophil extracellular traps- (NETs) 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

\$20.8M (3Q'22)



FINANCING

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



CASH RUNWAY

Cash Runway to 4Q'23



EQUITY OPPORTUNITIES

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



REVENUE

\$21.2M in revenue (YTD 2022)



NET BURN RATE

\$5.7 M/Q



DEBT

\$28.75M in debt (Convertible Notes) due Sept. 2024



SHAREHOLDER BASE

Strong institutional stockholder base

STOCK INFORMATION

NYSE American	PLX
Tel Aviv Stock Exchange	PLX
Outstanding Shares	50,665,598 ¹
Market Cap	\$55.8M ²

ANALYST COVERAGE

Raghuram Selvaraju, Ph.D.	H.C. Wainwright
John D. Vandermosten	Zacks

1. As of November 10, 2022.

2. Based on December 1, 2022 per share price.



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.

Accomplished Board of Directors



ZEEV BRONFELD

Chairman



DROR BASHAN

President & CEO, Director



POL F. BOUDES, M.D.

Director



GWEN A. MELINCOFF

Director



AHARON SCHWARTZ, PH.D.

Director



AMOS BAR SHALEV

Director



SHMUEL "MULI" BEN ZVI, PH.D.

Director

