PROTALIX Biotherapeutics

PROTALIX BIOTHERAPEUTICS

CORPORATE PRESENTATION

March 2024

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Investment Highlights

A strong foundation to further expand Into the Rare Disease space

Two Approved Drugs

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

Elfabrio® (pegunigalsidase alfa) has been approved for marketing by the FDA and the European Commission for Fabry disease.(1)

Clinical and Regulatory Expertise in Rare Genetic Space

Strong clinical and regulatory expertise for biologics and world-class network of Lysosomal Storage Disorder disease experts.

Clinically-Validated Platforms

Proprietary **ProCellEx® platform** for recombinant protein expression cGMP(2) manufacturing facility successfully inspected and audited by multiple regulatory agencies, including the FDA & EMA.

Development Pipeline

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

Strong Partnerships

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

Revenue-Generating

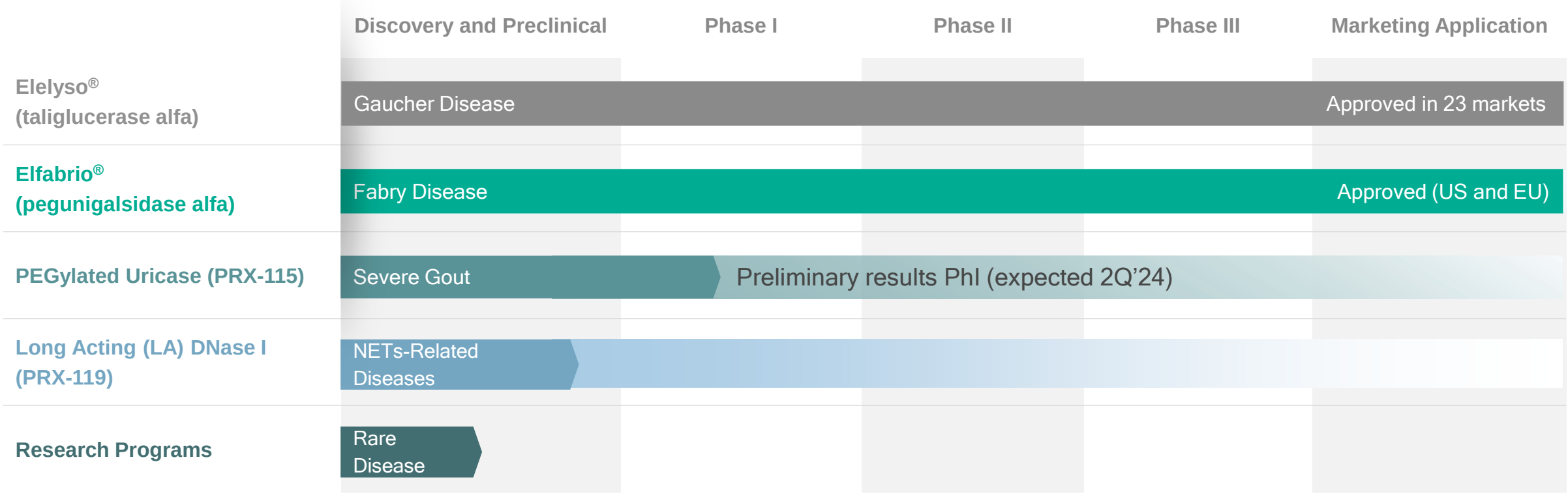
Multiple revenue streams, including sales to Pfizer, Fiocruz (Brazil) and Chiesi.

PROTALIX Biotherapeutics

(1) For the treatment of adult patients with Fabry disease
(2) 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



Note: Current pipeline candidates are recombinant proteins expressed via our proprietary ProCellEx® system

Elelyso® for Gaucher Disease

First plant cell derived recombinant protein approved by the FDA

Gaucher Disease

- **Rare autosomal recessive disorder:** affects 1 in 40,000 people
- **Glucocerebrosidase (GCD) enzyme deficiency** resulting in accumulation of glucosylceramide, a lipid, in bone marrow, lungs, spleen, liver, and sometimes brain

Symptoms and Treatment

- Possible **symptoms** include enlarged liver and spleen, various bone disorders, easy bruising and bleeding and anemia
- **Left untreated**, it can cause permanent body damage and decreased life expectancy
- **Standard of Care**: Enzyme Replacement Therapy

Product

elelyso® (taliglucerase alfa) for injection
Plant based. People focused.®

- **Elelyso** (alfataliglicerase in Brazil) is a proprietary, recombinant form of GCD for long-term treatment of patients with a confirmed diagnosis of type 1 Gaucher disease
- Expressed through our ProCellEx® platform

Commercial Potential

FDA APPROVED

- **Approved in 23 markets**
- Worldwide exclusive license agreement with Pfizer in 2009, amended in 2015 (excluding Brazil)
- Sales ~$10.4M in Brazil (FY2023) via Fundação Oswaldo Cruz
- Market share in Brazil: ~27%

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.

Elfabrio® for Fabry Disease

Second plant cell derived recombinant protein approved by the FDA

Fabry Disease

- **Rare X-linked disease:** affecting about one in every 40,000 to 60,000 men worldwide
- **α-galactosidase-A enzyme deficiency** leads to accumulation of the fatty substance globotriaosylceramide (Gb_3) in blood and blood vessel walls throughout the body

Symptoms and Treatment

- 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: Enzyme Replacement Therapy** (Replagal® or Fabrazyme®[1,2])

Product

- **Elfabrio** (pegunigalsidase alfa): Chemically Modified, Plant Cell Derived, PEGylated, Covalently Linked Homodimer
- **Approved for marketing by the EC, FDA and others**
- Expressed through our ProCellEx® platform

Commercial Potential

FDA APPROVED

EUROPEAN MEDICINES AGENCY

Chiesi

- Fabry: ~$2B (2023) expected to reach ~$3B (2030) Poised to capture significant global market share (15-20%)
- Will potentially be entitled to **$120M-$150M royalties per year** from Chiesi [3]

1. Does not include Galafold®, a small molecule drug indicated for adult Fabry patients with an amenable GLA variant.
2. Replagal is not approved in the US.
3. Based on projected 20-25% share of projected market size increase to ~$3 billion by 2030.

Fabry Disease Competitive Landscape

~$2B market (2022) expected to reach over $3.5B (2029), CAGR of 8.5%

Product Name	Fabrazyme®	Replagal®	Galafold®	Elfabrio®
Parent Company	sanofi	Takeda	Amicus Therapeutics	PROTALIX Biotherapeutics
Mechanism	ERT	ERT	Pharmacological chaperone	**ERT**
Approved for	Adults and pediatric patients 2+ years (U.S.); Adults, children and adolescents aged 8+ years. (E.U.)	Adults (E.U. only)	Accelerated approval in adults (U.S.) Adults and adolescents 16+ years (E.U.)	**Adults (U.S. and E.U.)**
Dosing	1 mg/kg every 2 weeks	0.2 mg/kg every 2 weeks	123 mg every other day	**1 mg/kg every 2 weeks**
Administration mode	Intravenous infusions	Intravenous infusions	Oral	**Intravenous infusions**
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.)	**2023 (U.S. and E.U.)**

Elfabrio is poised to capture meaningful global market share (15-20%)

Committed 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
- Strong sales and marketing partner poised to maximize the market potential of pegunigalsidase alfa as the centerpiece of their new strategic U.S.-based Orphan Drug division

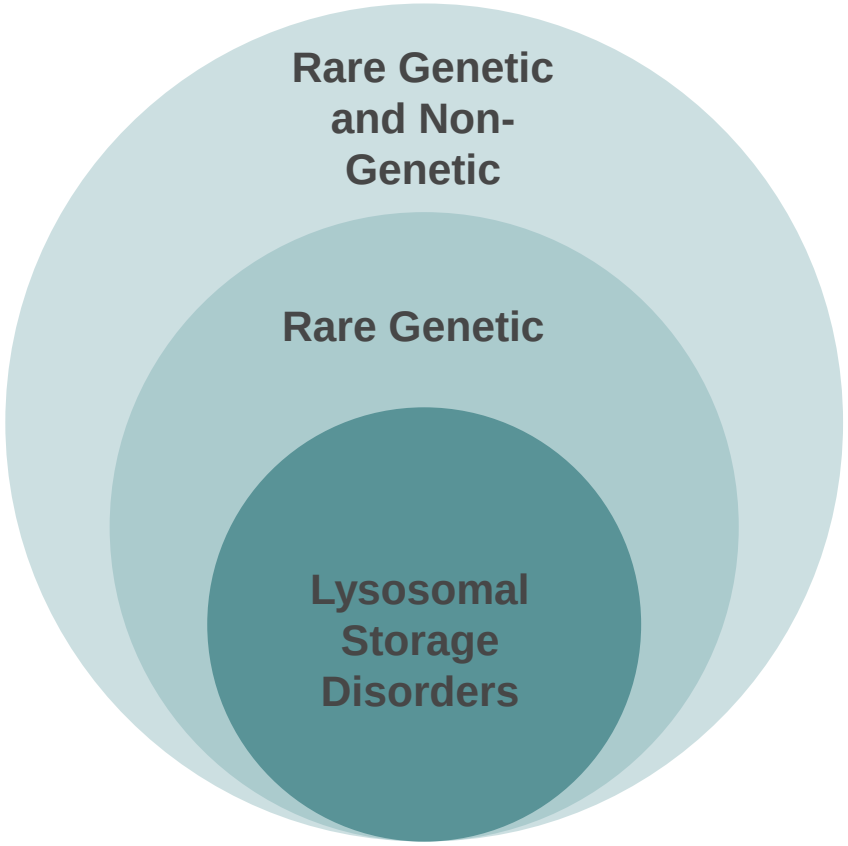
- Committed global partner with experienced sales team
- Strategic focus on rare diseases
- Specific expertise in Fabry disease
- Ideally suited to bring Elfabrio® to patients with Fabry disease(1)

(1) Tiered royalties of 15-35% (ex-US); 15-40% (U.S.)

Growing Focus on High Unmet Needs in Rare Disease Space

Focus on Rare Disease space

Goal: *Within 2 years, 4-6 discovery to PhII programs in the pipeline*



Our Strategy: Focus on Rare Disease space

- Both genetic and non-genetic opportunities
- Prioritize opportunities with LCM potential
- Diseases with high unmet needs
- Surrogate endpoints/biomarkers

Systematic Approach to BD&L Screen

- Significant in-licensing to build a sustainable portfolio
- Open to modalities outside protein (exc. CGT)
- **Protalix has initiated a large BD&L process to bring in novel opportunities in the rare disease space**
- Protalix is also reviewing **emerging innovative platforms**

In-House Discovery Pipeline based on Protein Capabilities

- Leveraging ProCellEx platform and PEGylation capabilities for highly innovative opportunities
- Reinforce protein capabilities

CGT = Cell and Gene Therapies; LCM = Life cycle management

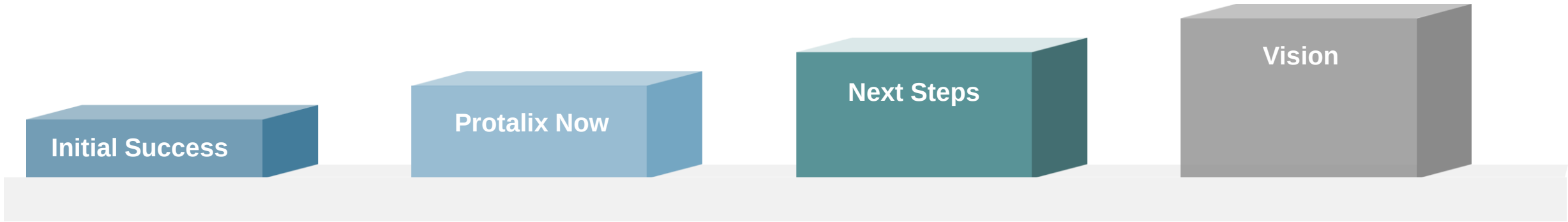
Evolving Protalix: Addressing High Unmet Needs in the Rare Disease Space

Leveraging track record of success into other rare diseases

Strategy

Track Record of Success in Rare Genetic Space

Striving for Continued Success in Rare Diseases (genetic and non-genetic)



May 2012:

Protalix's 1st approved product

elelyso® (taliglucerase alfa) for injection
Plant based. People focused.®

May 2023:

Protalix's 2nd approved product

ELFABRIO® (pegunigalsidase alfa-iwxj)

Within 2 years, 4-6 discovery to PhII programs

Reinforce **Protein Discovery Capabilities**

BD&L: Preclinical/Clinical Pipeline

Develop **highly innovative rare disease treatments** addressing real unmet needs

Building a **significant pipeline with innovative rare disease clinical programs**

Fully Integrated with End-to-End capabilities

Commercial infrastructure to support novel products

Leveraging **novel technology platforms** with broad potential in rare diseases

PROTALIX Biotherapeutics

Well Capitalized to Advance Protalix to Next Phase

CASH
$44.6M (FY 2023)

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'25[1]

1.Based on current cash and cash equivalents and expected receipt of milestones; based on a number of assumptions and may vary significantly from our expectations. See Forward Looking Statements.

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

REVENUE
$65.5M in revenue (FY 2023)

NET BURN RATE
Projected: 0 to +$1.5 M/Q

DEBT
$20.4M in debt (Convertible Notes) due Sept. 2024

STOCKHOLDER BASE
Strong institutional stockholder base

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.

SHOSHI TESSLER, PH.D.
VP, Clinical Development & Regulatory Affairs

Dr. Tessler joined Protalix in October 2023. She has over 20 years of experience in the pharmaceutical industry, leading a broad range of innovative drug development projects and activities, from lead-stage to phase III clinical trials and marketing applications. Prior to Protalix, she served as VP, R&D of Biosight Ltd. and of Enzymotec Ltd. (currently part of International Flavors & Fragrances Inc.) and as a Sr. Director Project Champion at Innovative R&D of Teva.

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.

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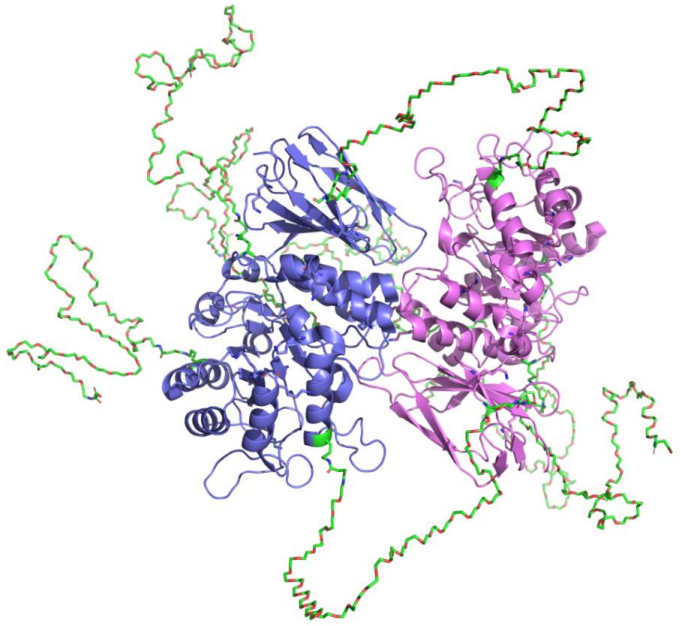
Appendix

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)
- Continued of an alternative dosing regimen with potential for once every 4 weeks dosing



2kD PEG

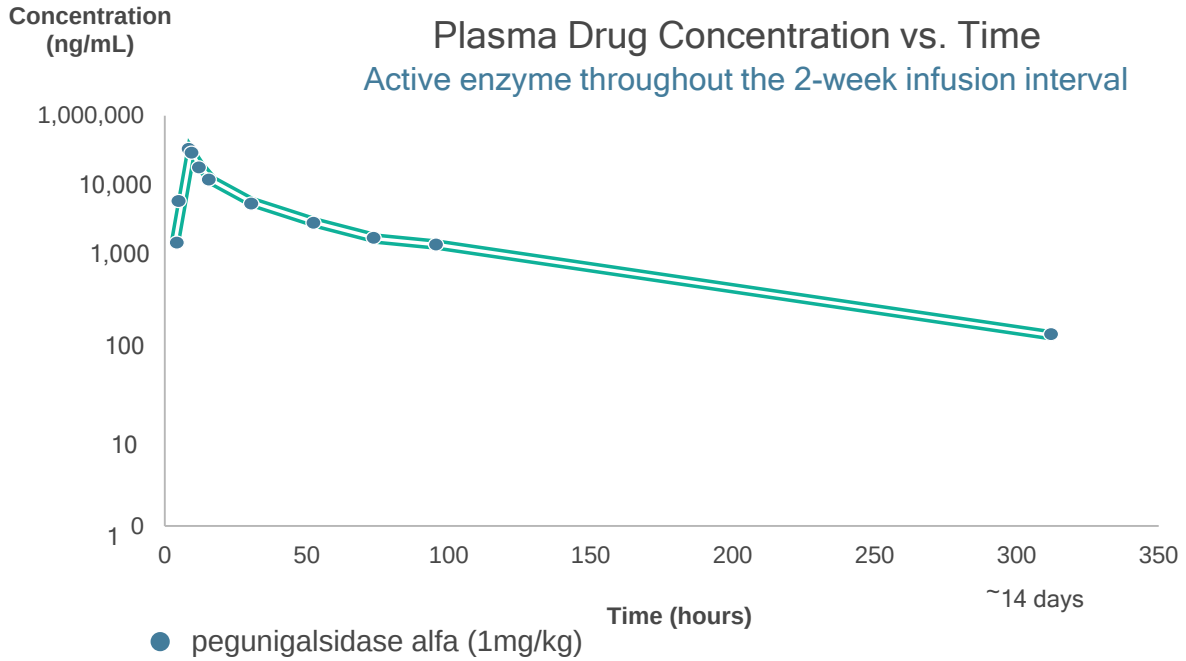
Ruderfer I., et al. Development and Analytical Characterization of Pegunigalsidase Alfa, a Chemically Cross-Linked Plant Recombinant Human α-Galactosidase-A for Treatment of Fabry Disease. Bioconjug Chem. 2018 (pp. 1-8)

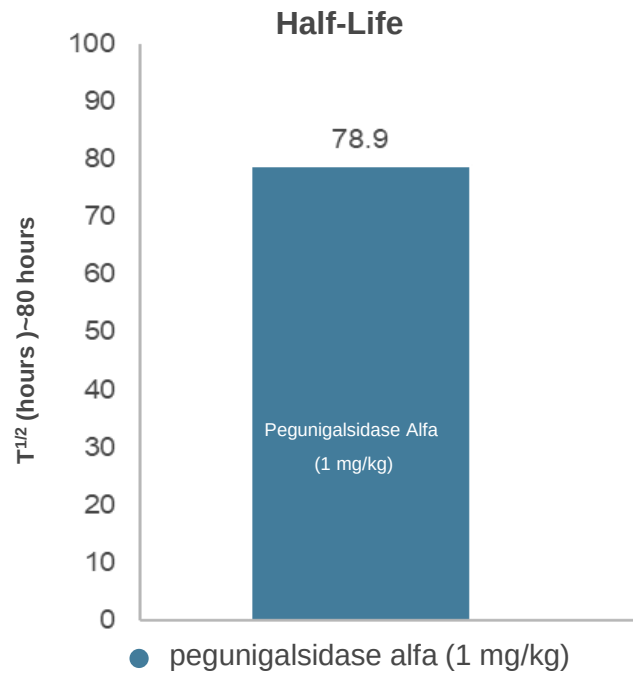
Schiffmann R., et al. Pegunigalsidase alfa, a novel PEGylated enzyme replacement therapy for Fabry disease, provides sustained plasma concentrations and favorable pharmacodynamics: A e 1/2 clinical trial. J of Inherited Metabolic Disease. 2019 (pp. 534-544)

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 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 • 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

Summary of Clinical Activity Data from Phase III Clinical Program

Program demonstrates 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 -5.90 to -1.19 mL/min/1.73m^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 ±3.35) to Week 52 (22.23 nM ±3.60)
- 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

- The median (95% confidence interval) of the eGFR slope in the pegunigalsidase alfa 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 III Clinical Program

All trials to date show favorable tolerability and immunogenicity profiles

bridge	bright	balance
Patient population (n=22)	Patient population (n=30)	Patient population (n=78)
Favorable tolerability profile	Favorable tolerability profile	Favorable tolerability profile
Most TEAEs were mild or moderate in severity, with all AEs being transient	No increase or relapse in pain reported	Less related TEAEs in PRX-102-treated patients (42 vs. 76 events or 42.85 vs. 152.91 adjusted to 100 treatment years)[1]
2 patients (9.1%) withdrew from treatment due to an SAE (hyper-sensitivity reaction (resolved following withdrawal)	No de novo ADAs were reported following switch to PRX-102	Number of infusion-related reactions (IRR) adjusted to 100 infusions in the pegunigalsidase alfa arm was 0.5 vs. 3.9 in the agalsidase beta arm
Favorable immunogenicity profile	Favorable immunogenicity profile	Favorable immunogenicity profile, with the proportion of patients with neutralizing ADA declined over time with pegunigalsidase alfa but not with agalsidase beta

(1) Compared to agalsidase beta

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 (88 treated)[1]
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)[1]

NCT04552691 — Expanded Access Program in the US – Currently Enrolling

1. As of April 30, 2023

European Commission Granted Marketing Authorization to pegunigalsidase alfa

Pegunigalsidase alfa 1 mg/kg every two weeks is indicated for long-term enzyme replacement therapy in adult patients with a confirmed diagnosis of Fabry disease (deficiency of alpha-galactosidase)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Chiesi

Safety

The clinical safety profile is overall comparable to that of other authorized ERTs for Fabry disease

No unexpected safety concerns observed in intended population

Observed infusion-related reactions adverse events seem overall manageable, in particular with premedication

Pharmacodynamics

The pharmacodynamic profile showed a beneficial effect in ERT naïve patients, decreasing both Gb_3 inclusion bodies and plasma Lyso-Gb_3 levels

Plasma Lyso-Gb_3 levels stayed stable in pretreated patients after 24 months of treatment

Efficacy

The clinical efficacy as measured by annualized eGFR showed:

- Renal function trend of improvement in main study
- Patients deteriorated less rapidly compared to previous treatment (agalsidase alfa) in single arm study
- Long term effect of treatment maintained in integrated analysis

No final conclusion on non-inferiority over agalsidase beta can be made; however, the demonstration of efficacy is based on: (i) the known nature of ERT in Fabry, (ii) the well-understood MOA, (iii) pharmacodynamic effects observed that would not be expected without ERT and (iv) some clinical effect on renal function

Based on the totality of the data, the overall benefit/risk balance of pegunigalsidase alfa is positive