



PROTALIX  
Biotherapeutics

# PROTALIX BIOTHERAPEUTICS

CORPORATE PRESENTATION

May 2025

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# Investment Highlights

## Established commercial foundation fuels further expansion into the Rare Disease space



### Commercial Portfolio

Ellelyso<sup>®</sup> (alfataliglicerase in Brazil): FDA approved, commercially marketed drug for Gaucher disease  
Elfabrio<sup>®</sup> (pegunigalsidase alfa) FDA/European Commission<sup>1</sup> approved for marketing for Fabry disease<sup>2</sup>



### ProCellEx<sup>®</sup> Clinically-Validated Platform

Proprietary platform for recombinant protein expression  
cGMP<sup>3</sup> facility provides efficient, flexible genetic engineering/manufacturing  
Audited by multiple regulatory agencies, including the FDA & EMA



### Expertise in Rare Genetic Disease Space

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



### Revenue Generating Partnerships

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

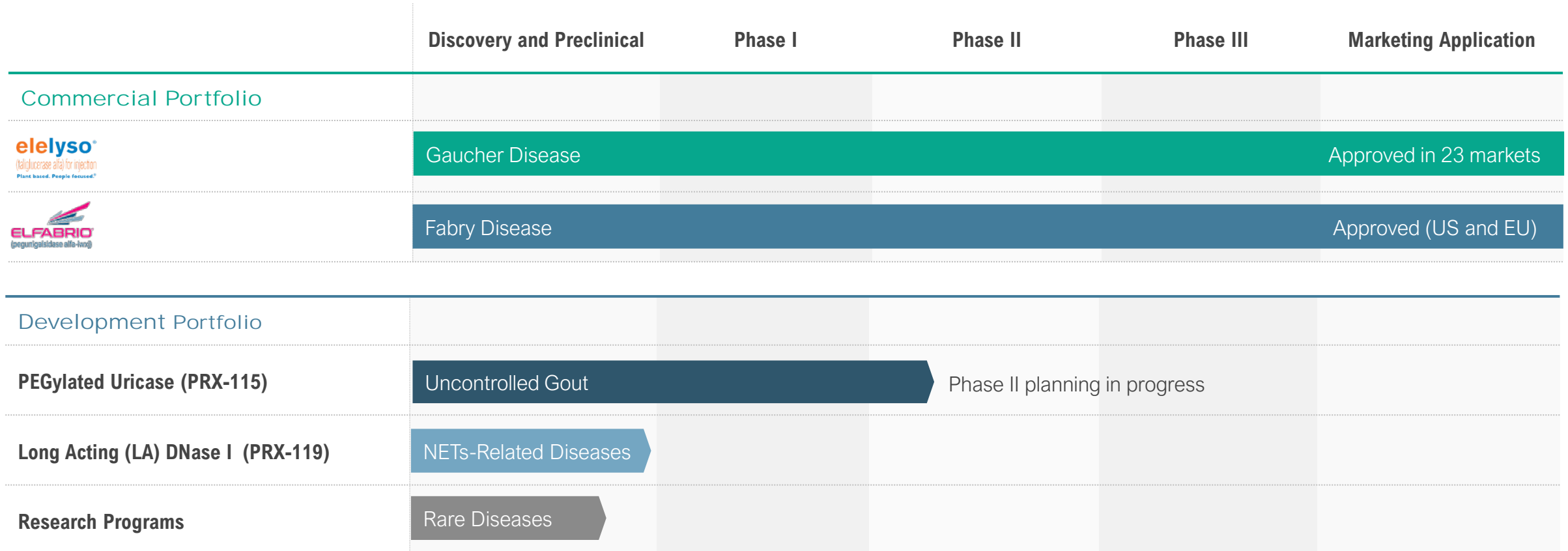


### Promising Development Portfolio

PRX-115: Uricase for uncontrolled gout advancing toward Phase 2  
PRX-119: Long-acting DNase I for NETs-related diseases  
Multiple other product candidates, in discovery and preclinical phases

# Product Pipeline

Recombinant proteins designed to potentially target unmet medical needs in established pharmaceutical markets



Development candidates are generally recombinant proteins expressed via our proprietary ProCellEx® system

# Commercial Portfolio



# 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

### Product

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<sup>®</sup> platform

### 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

### Commercial Potential

Approved in 23 markets<sup>1</sup>

Worldwide exclusive license agreement with Pfizer in 2009, amended in 2015 (excluding Brazil)

Sales ~\$11M in Brazil (FY2024) via Fundação Oswaldo Cruz

Market share in Brazil: ~25%



# 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

$\alpha$ -galactosidase-A enzyme deficiency leads to accumulation of the fatty substance

globotriaosylceramide (Gb<sub>3</sub>) in blood and blood vessel walls throughout the body

### 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<sup>®</sup> platform

### 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<sup>®</sup> or Fabrazyme<sup>®</sup> 1,2)





### Commercial Potential

Fabry: ~\$2.2B (2024) expected to reach ~\$3.1B (2030); Poised to capture significant global market share (15-20%)

Protalix royalties per year from Chiesi (15% to 35% tiered Ex-US, 15% to 40% tiered US)

# Fabry Disease Competitive Landscape

~\$2.2B market (2024) expected to reach over \$3.1B (2030), CAGR of 6.6%

Product Name	Fabrazyme®	Replagal®	Galafold®	Elfabrio®
Parent Company				
Mechanism	ERT	ERT	Pharmacological chaperone	ERT
Approved for	Adults & pediatric patients 2+ years (US); Adults, children and adolescents aged 8+ years. (EU)	Adults (EU only)	Accelerated approval in adults (US). Adults and adolescents 16+ years (EU)	Adults (US, EU and others)
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 2 mg/kg every 4 weeks
Administration mode	Intravenous infusions	Intravenous infusions	Oral	Intravenous infusions
Approval Date	Full approval in 2021; accelerated approval in 2003 (US); 2001 (EU)	Not approved in US; 2001 (EU)	2018 (US); 2016 (EU)	1 mg/kg 2023 (US and EU) 2 mg/kg EMA acceptance of review December 2024

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

# Global Partnership with Chiesi

## Committed Global Partner

- International research-focused biopharmaceutical group with sales in excess of €3.4B in 2024 (reflecting 13% growth year-on-year)
- Operating in over 30 countries with over 7,000 employees
- Strong sales and marketing partner poised to maximize the market potential of pegunigalsidase alfa as the centerpiece of their new strategic US-based Rare Disease division
- Elfabrio<sup>®</sup> launches underway in US, throughout EU and additional markets
- Rich tiered royalties agreement (Ex-US 15-35%; US 15-40%) and potential significant commercial and regulatory milestones (multiple hundreds of million dollars)
- Potential forecasted annual net sales<sup>1</sup> from Chiesi exceeding \$100M by 2030 (representing 15-20% of the global Fabry market)

### Chiesi Farmaceutici S.p.A.

- Experienced sales team
- Strategic focus on rare diseases
- Specific expertise in Fabry disease
- Ideally suited to bring Elfabrio to patients with Fabry disease





## Development Portfolio

PRX-115 in Development for  
Uncontrolled Gout

# Gout

## Most Common Inflammatory Arthritis

Gout affects approximately 15 million people in the US

~5% (estimated) of the gout population is considered to have chronic refractory gout

## Accumulation of Excess Uric Acid

Hyperuricemia leads to accumulation of urate crystals (tophi) almost anywhere in the body, including bones and joints, as well as organs such as the heart and kidney

Triggers recurrent episodes of sudden, pronounced acute inflammation, known as gout flares

## Systemic Disease

Symptoms: severe acute pain, inflammation, stiffness, limited range of motion

Co-morbidities: hypertension, cardiovascular disease, renal impairment, diabetes, obesity, hyperlipidemia, and frequently in a combination known as the metabolic syndrome

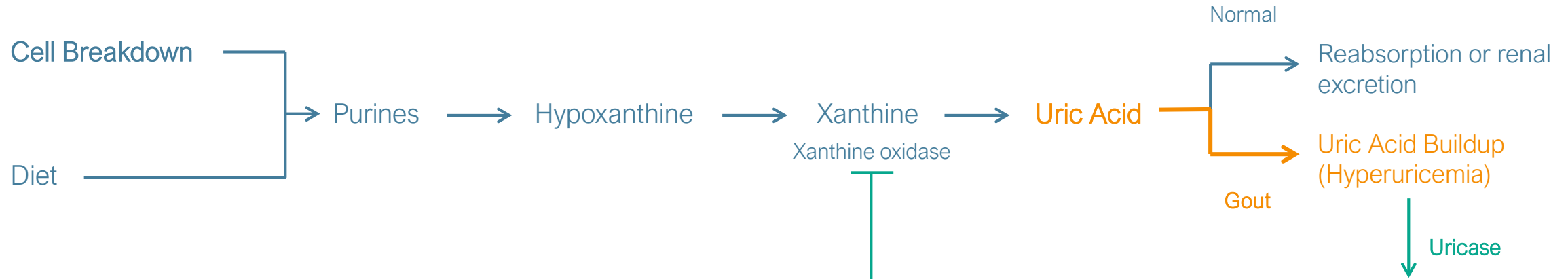
## Currently Available Therapies

First-line xanthine oxidase inhibitors (XOIs): Allopurinol and Febuxostat

One recombinant uricase approved for chronic gout in adult patients refractory to conventional therapy as every two-week injection: Krystexxa<sup>®1</sup>

# Currently Available Urate-Lowering Therapies

## Unmet needs remain in uncontrolled gout patients



### Xanthine Oxidase Inhibitors (XOIs):

Allopurinol  
Febuxostat

First-line oral treatment

Reduces uric acid levels by blocking its synthesis

*However, uncontrolled gout patients typically do not reach target uric acid levels with XOI treatment alone and experience recurrent flares*

### Recombinant Uricase:

Approved for refractory gout

IV infusion every two weeks

Eliminates excess uric acid

*However, it has an extensive side effect profile due to anti-drug antibodies, requiring combination with methotrexate<sup>1</sup>*

**KRYSTEXXA**  
pegloticase

# PRX-115: Significant Potential in Uncontrolled Gout

## Uncontrolled Gout (Unmet Need)

An estimated 5% of the gout population is considered to have chronic refractory disease

Uncontrolled gout patients typically do not reach target uric acid levels with (XOI) treatment alone and experience recurrent, painful flares

There remains an unmet need for treatment options for patients with uncontrolled gout who are not able to lower uric acid levels, or who experience unwanted side effects with currently available treatments

PRX-115 may represent a much-needed alternative treatment option for uncontrolled gout

**\$5.6B**

Global Gout Market<sup>1</sup>

Expected CAGR of

**6.4%**

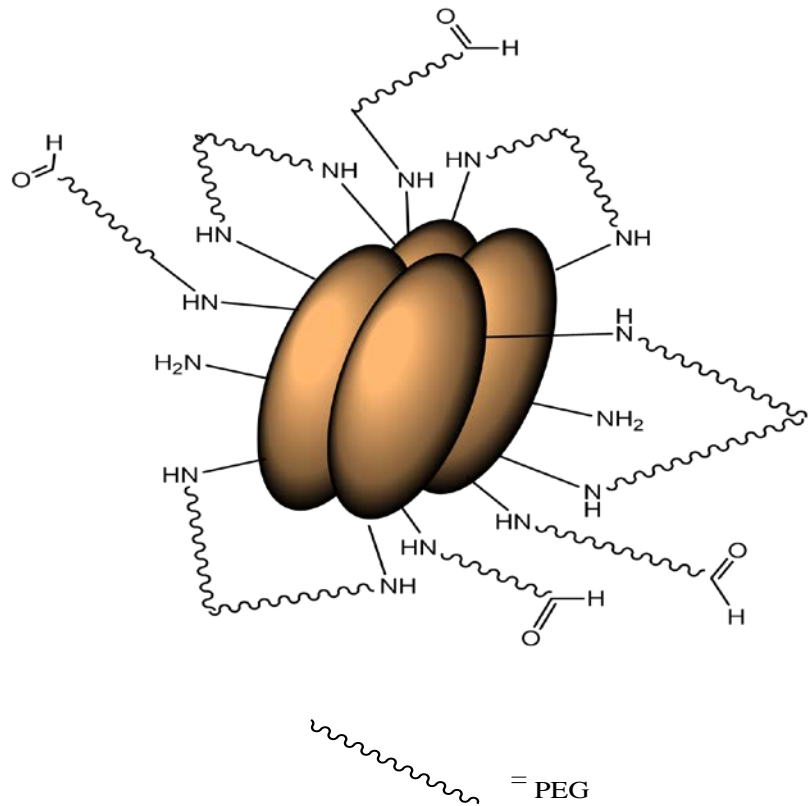
from 2022–2029

Krystexxa sales were

**\$1.2B**

in 2024

# PRX-115: Chemically Modified, Plant Cell Derived, PEGylated, Covalently Linked Homotetramer



3.4kD PEG

- PRX-115 is a PEGylated enzyme designed to potentially have lower immunogenicity by masking immunogenic epitopes and an improved safety profile
- PRX-115 is a plant cell-based recombinant *Candida Utilis* Uricase with substitution of Cystein to Lysin at position 250 that prevents enzyme aggregation and di-sulfide bond formation between the Uricase tetramers
- Chemically modified using proprietary modification with 40x 3.4 kDa Bis-Ald PEG molecules, resulting in cross-linking between subunits and >99.5% of backbone masking for reducing immunogenicity, increasing half-life and retaining efficacy

# PRX-115 Phase I Single Ascending Dose Study Design

## Study Scheme

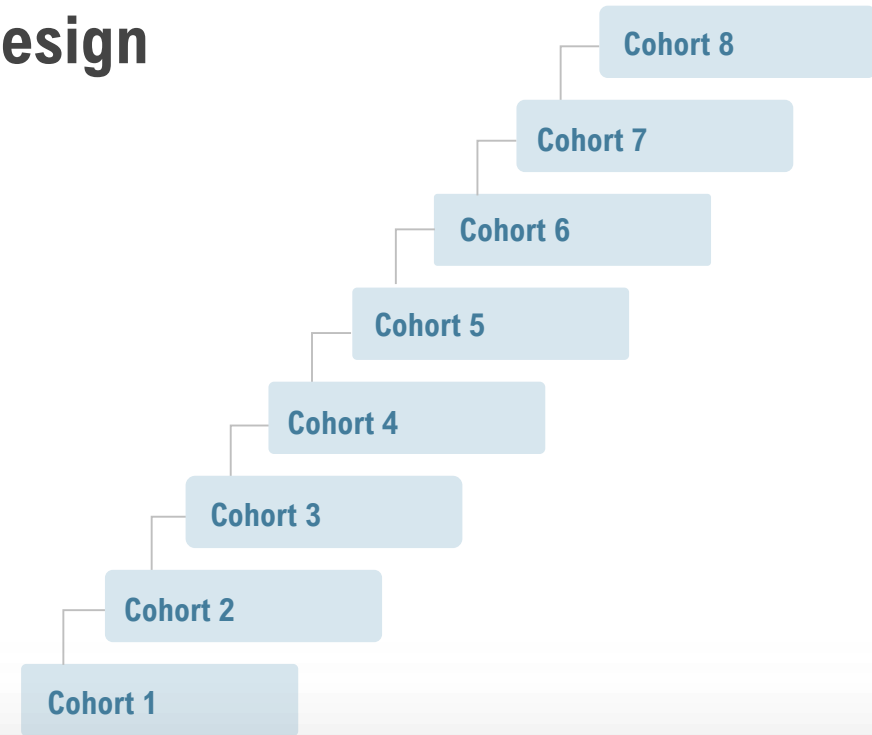
Primary Endpoint: safety and tolerability

Secondary Endpoints: PK, PD (uric acid levels)

Dose escalation meeting by blinded Safety Monitoring Committee (SMC) following completion of each cohort

N = 8 per cohort (6 PRX-115 + 2 placebo)

For subject safety, each cohort/dose level started at least 7 days from the dosing of the previous cohort



## Study schedule per patient



# PRX-115 Phase I Single Ascending Dose Study Summary

First-in-Human trial enrolled 64 subjects with elevated uric acid levels across 8 dose cohorts

## Safety and Immunogenicity

Phase 2 Planning In Progress

Favorable tolerability profile

12 of 48 PRX-115-treated subjects experienced a study drug-related adverse event (AE)

Majority of study drug-related AEs were mild to moderate and transient in nature

One subject in cohort 2 experienced an immediate anaphylactic reaction; fully resolved

No other serious AEs were reported

No related AEs were reported in dose cohorts 6 and 7

PRX-115 immunogenicity is still under evaluation, including correlation to PK, PD and safety

## PK / PD

Phase 2 Planning In Progress

PRX-115 exposures increased in dose-dependent manner

Detectable PRX-115 levels were observed in plasma for up to 12 weeks from subjects in cohorts 6, 7 and 8

Rapid reduction of plasma uric acid levels to below 6.0 mg/dL

Reduction of plasma uric acid occurred in dose-dependent manner and lasted beyond 4 weeks

# PRX-115 Summary

## Recombinant PEGylated Uricase Enzyme for Potential Treatment of Uncontrolled Gout

### Addressable Market

Approximately 15 million US gout patients, of which ~5% considered to have chronic refractory disease

### Status

Phase I First-in-Human study completed (8 cohorts); data is locked and currently being analyzed

Phase II planning in progress

### Next Steps

Phase II study in uncontrolled gout patients--initiation anticipated in 2H 2025



### Asset Overview

- Recombinant PEGylated uricase enzyme produced via ProCellEx<sup>®</sup> plant cell-based expression system
- Favorable tolerability profile demonstrated by preliminary phase I data for subjects with elevated uric acid levels
- Demonstrated stable PK profile, long half-life in preliminary phase I data
- Demonstrated ability to reduce uric acid levels to recommended guideline of below 6.0 mg/dL



### Market Overview

~\$1.4B market for gout overall and growing

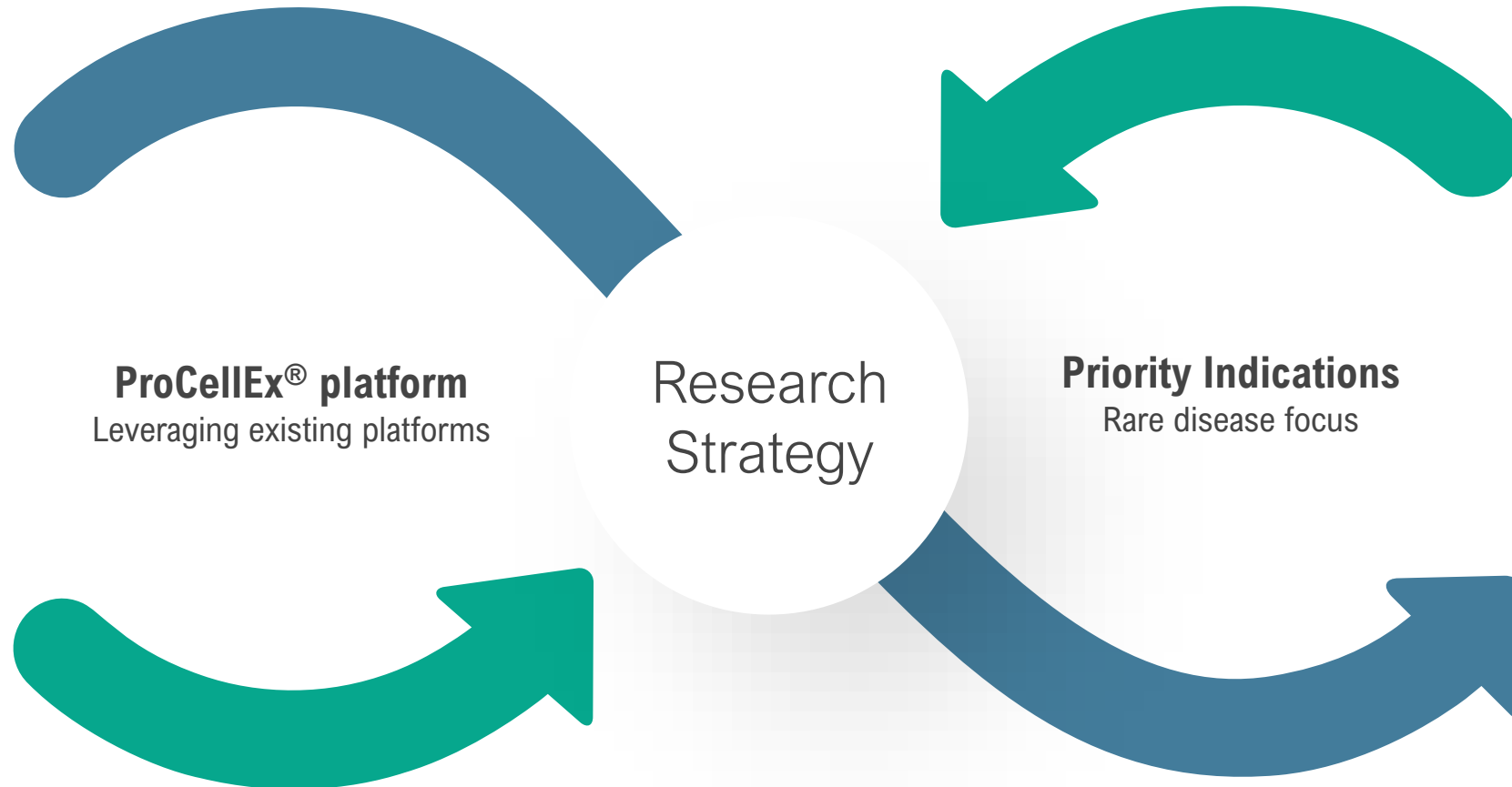
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# Growth Strategy

# Research to Fuel Next Stage of Growth

Goal: Within 3 years, 4-5 discovery to Phase II programs in the pipeline



# Expansion of ProCellEx<sup>®</sup> Platform for Drug Delivery

## Exploring platform expansion to include drug delivery modalities for optimized delivery of therapeutic proteins

- Unmet need: efficient and targeted delivery of therapeutic proteins
- Potential applications:
  - Package recombinant proteins in delivery modalities produced in the ProCellEx platform
  - Package other cargos (e.g., ASO/siRNAi) in delivery modalities derived from ProCellEx platform (potential academic/industry collaborations) and/or Biotech companies
  - Unlocking additional indications:
    - Specific targeting for delivery to certain organs to address tissue-specific unmet need
- Initial validation and feasibility studies in progress

**ProCellEx Platform**



**Protein therapeutics:**  
Plant cell-based expression

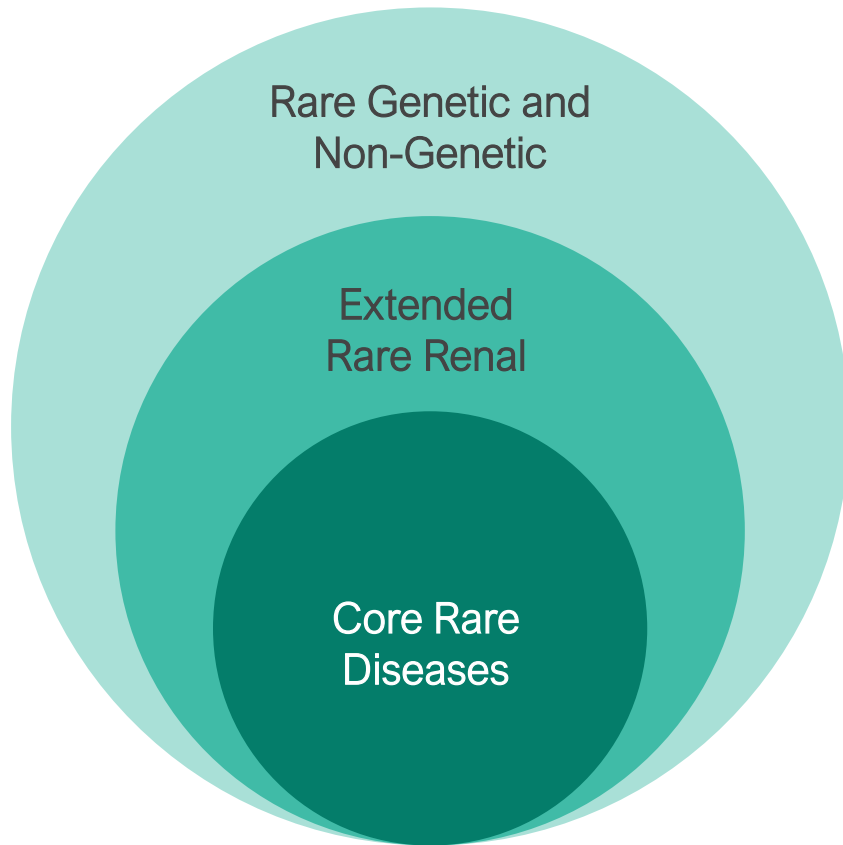


**Chemical modification:**  
PEGylation



**Drug delivery:**  
Exploring new modalities

# Focus on High Unmet Needs in Rare Disease Space



## Therapeutic Area Strategy: Focus on Rare Disease Space

- Protalix conducted systematic analysis to identify potential key areas of focus in rare disease space
- Both genetic and non-genetic opportunities
- Potential to prioritize rare renal diseases as the core of Protalix's development pipeline
- High unmet renal diseases include: ADPKD, Alport syndrome, FSGS and others

## Systematic Approach to BD&L

- Proactive BD&L strategy to complement internal portfolio, exploring:
  - Regular deal making, academic/ industry collaborations, development of internal expertise
- Protalix is also reviewing emerging innovative platforms

# Well Capitalized to Advance Protalix to Next Phase

## CASH STREAMS FROM STRONG PARTNERSHIPS

\$10.0 in Q1 2025 revenue from selling goods, up 17% over Q1 2024



## REVENUE

\$53M in revenue (FY 2024)



## CASH & CASH RUNWAY

\$34.7M (at March 31, 2025); approaching cash flow positive, sufficient to support ongoing operations<sup>1</sup>



## DEVELOPMENT PORTFOLIO DRIVES FUTURE GROWTH

PRX-115 recombinant PEGylated uricase product candidate. First-in-human Phase 1 data presented at ACR Nov 2024. Potential for differentiated wide dosing interval



## NO DEBT & NO WARRANTS



# 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 Dev & 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.



**ORI KALID, PH.D.**  
VP of R&D

Dr. Ori Kalid joined Protalix as Vice President of Research and Development in June 2024, bringing over 20 years of leadership experience in multidisciplinary pharmaceutical R&D. Before joining Protalix, Ori co-founded and served as the CEO of SILVERSKATE BIO, an immunology startup. He was co-founder and CEO of Pi Therapeutics, also served at Hotaru Innovation Partners, PREDIX/EPIX pharmaceuticals and Karyopharm Therapeutics.

# Accomplished Board of Directors



**ELIOT FORSTER, PH.D.**  
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





# Appendix

## Participant Demographics and Baseline Characteristics

Parameter	Statistic	Pooled PRX-115	Pooled Placebo	Overall
Age (years)	n	48	16	64
	Mean	35.9	33.4	35.3
	SD	12.3	10.8	11.9
Sex n(%)	Female	16(33.3)	5(31.3)	21(32.8)
	Male	32(66.7)	11(68.8)	43(67.2)
Race n(%)	American Indian or Alaska Native	0	0	0
	Asian	7(14.6)	5(31.3)	12(18.8)
	Black or African American	1(2.1)	0	1(1.6)
	Native Hawaiian or other Pacific Islander	8(16.7)	2(12.5)	10(15.6)
	White	31(64.6)	8(50.0)	39(60.9)
	Other	3(6.3)	2(12.5)	5(7.8)
Weight (kg)	Mean	87.52	85.87	87.11
	SD	18.06	18.37	18.01
Body Mass Index (kg/m <sup>2</sup> )	Mean	29.16	28.01	28.87
	SD	5.03	5.35	5.10
Plasma Urate (mg/dL)	Mean per cohort	7.0-8.5	7.0	7.0-8.5

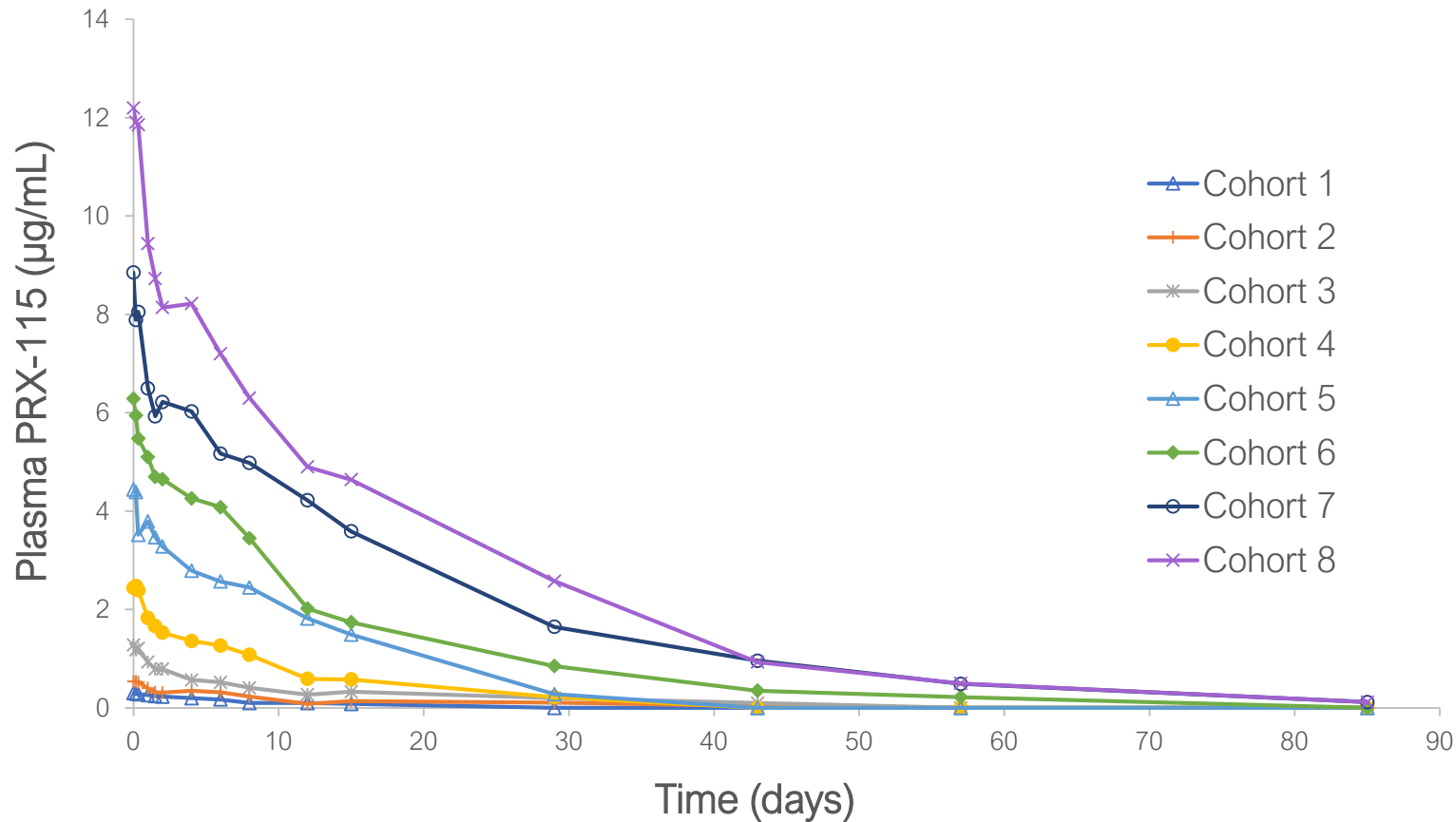
## Overall Summary of Adverse Events\*

	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Cohort 8	Pooled PRX-115	Pooled Placebo
<b>N</b>	6	6	6	6	6	6	6	6	48	16
<b>TEAE n(%)</b>	5(83.3)	6(100.0)	5(83.3)	3(50.0)	6(100.0)	5(83.3)	3(50.0)	4(66.7)	37(77.1)	13(81.3)
<b>Related TEAE n(%)</b>	1(16.7)	5(83.3)	3 (50.0)	1(16.7)	1(16.7)	0	0	1(16.7)	12(25.0)	3(18.8)
<b>Serious Related TEAE n(%)</b>	0	1(16.7)	0	0	0	0	0	0	1(2.4)	0
<b>TEAE Leading to Study Drug Discontinuation n(%)</b>	0	1(16.7)	0	0	0	0	0	0	1(2.1)	0
<b>TEAE Leading to Study Discontinuation n(%)</b>	0	0	0	0	0	0	0	0	0	0

# PRX-115 Pharmacokinetic Profile

Dose-dependent increase in PRX-115 exposure with single administration

## PRX-115 Mean Plasma Concentrations Throughout 85-day Follow-up Period (n=48)

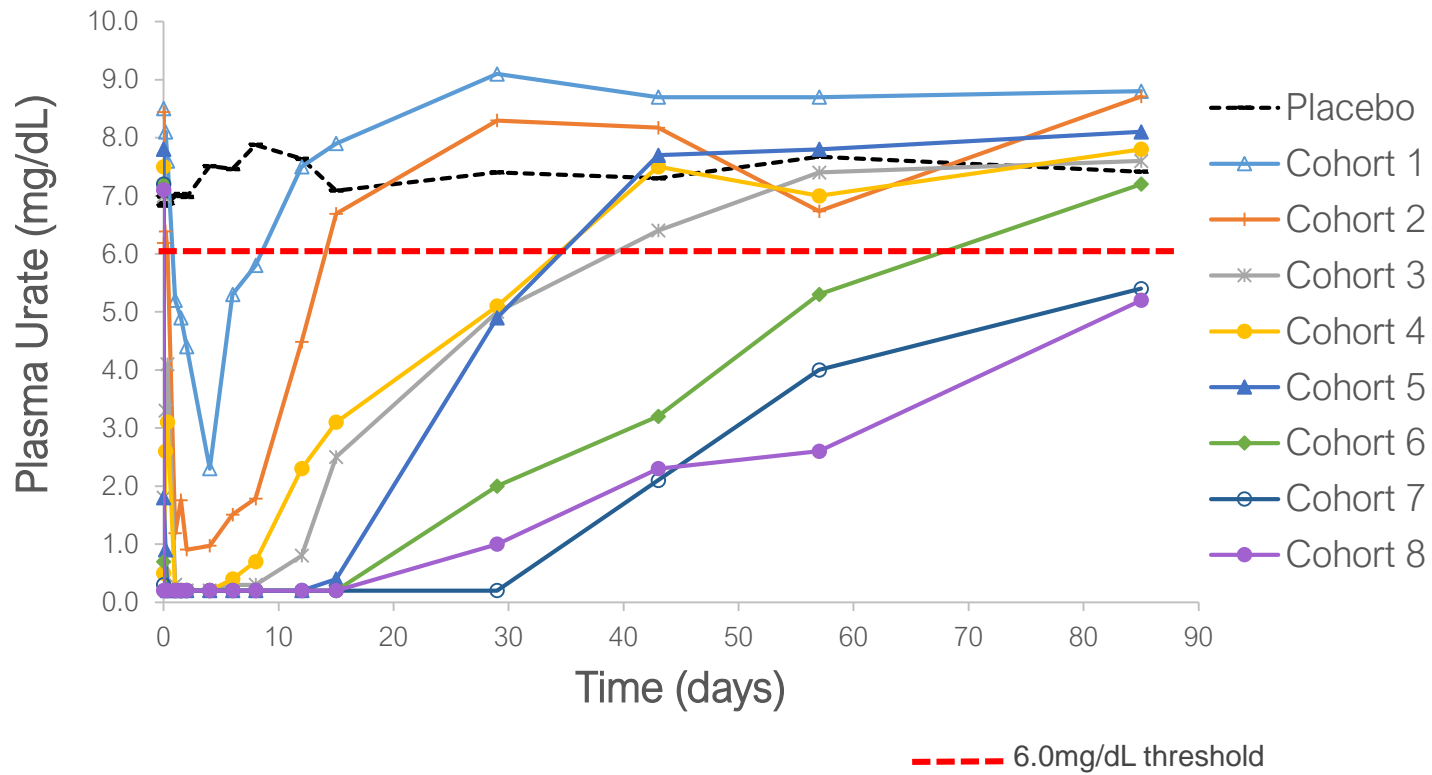


Detectable exposures were observed in plasma for up to 12 weeks in participants in highest dose cohorts 6, 7 and 8

# PRX-115 Pharmacodynamic Results

Rapid reduction of plasma uric acid below 6 mg/dL following single administration of PRX-115

## Uric Acid Mean Plasma Concentrations Throughout 85-day Follow-up Period (n=64)



Effect of PRX-115 on plasma uric acid levels and duration of response is dose dependent

Plasma urate levels remained below 6.0 mg/dL for up to 12 weeks at the highest dose levels

Cohort 2 excludes one patient who received 5% of the full dose.