



PROTALIX  
Biotherapeutics

# PROTALIX BIOTHERAPEUTICS

CORPORATE PRESENTATION

June 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<sup>1</sup>



## 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<sup>2</sup> manufacturing facility successfully inspected and audited by multiple regulatory agencies, including the FDA & EMA



## Growing Development Pipeline

PRX-115: Uricase for uncontrolled gout

PRX-119: Long Acting DNase I for NETs-related diseases

Multiple other product candidates, in discovery and preclinical phases



## Strong Partnerships

Chiesi Farmaceutici S.p.A.

Pfizer Inc.

Fundação Oswaldo Cruz (Fiocruz)



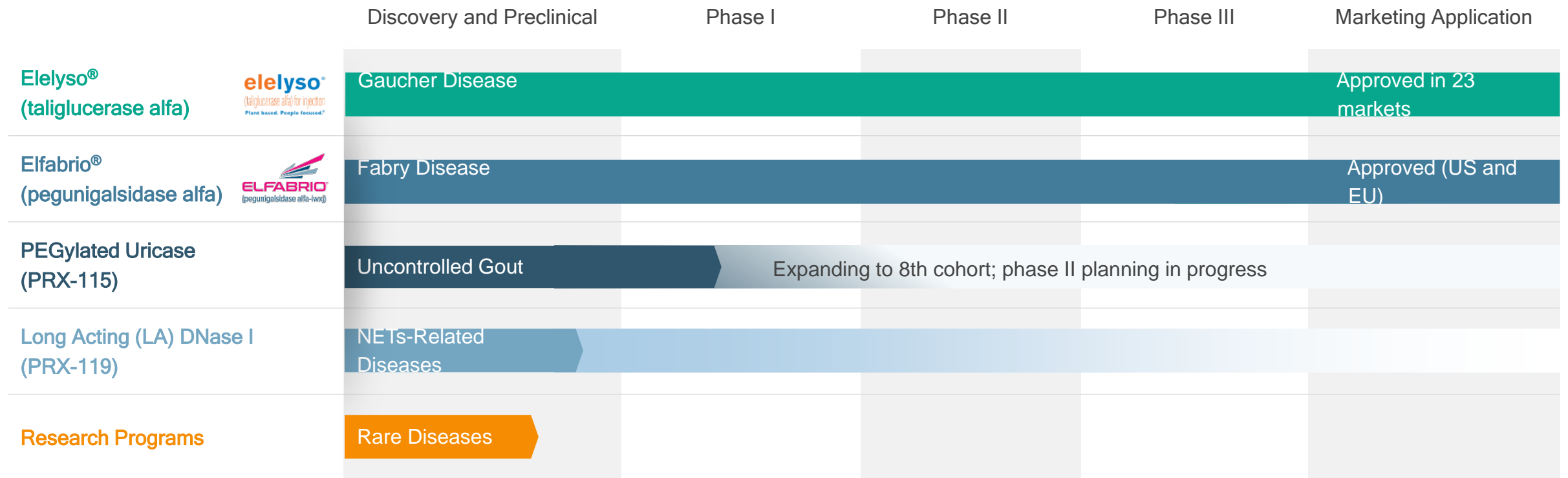
## Revenue-Generating

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



# 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 generally recombinant proteins expressed via our proprietary ProCellEx® system



## Approved Products



# Elelyso<sup>®</sup> 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 (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

## Commercial Potential



- 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%

# Elfabrio<sup>®</sup> 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

## Symptoms and Treatment



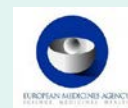
- Progressive disease that can lead to renal failure, cardiomyopathy with potentially malignant cardiac arrhythmias, and strokes
- Symptoms such as abdominal and neuropathic pain can appear in patients as young as two years old
- Standard of Care: Enzyme Replacement Therapy (Replagal<sup>®</sup> or Fabrazyme<sup>®1,2</sup>)

## 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

## Commercial Potential







- Fabry: ~\$2B (2023) expected to reach ~\$3.1B (2030); Poised to capture significant global market share (15-20%)
- Will potentially be entitled to \$120M-\$150M royalties per year from Chiesi<sup>3</sup>



# Fabry Disease Competitive Landscape

~\$2B market (2023) expected to reach over \$3.1B (2030), CAGR of 6.8%

Product Name	Fabrazyme®	Replagal®	Galafold®	Elfabrio®
Parent Company				
Mechanism	ERT	ERT	Pharmacological chaperone	ERT
Approved for	Adults and 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)	<b>Adults (US, EU and others)</b>
Dosing	1 mg/kg every 2 weeks	0.2 mg/kg every 2 weeks	123 mg every other day	<b>1 mg/kg every 2 weeks</b>
Administration mode	Intravenous infusions	Intravenous infusions	Oral	<b>Intravenous infusions</b>
Approval Date	Full approval in 2021; accelerated approval in 2003 (US); 2001 (EU)	Not approved in US; 2001 (EU)	2018 (US); 2016 (EU)	<b>2023 (US and EU)</b>

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 biopharmaceutical group with sales in excess of \$3B in 2023 (reflecting 10% growth year-on-year)
- Operating in close to 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 Orphan Drug division
- Elfabrio® launches underway in US, throughout EU and additional markets



- 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<sup>1</sup>





PRX-115 in  
Development for  
Uncontrolled Gout

# Gout



## Most Common Inflammatory Arthritis

Gout affects approximately 14 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>

# PRX-115: Significant Potential in Uncontrolled Gout

**Uncontrolled Gout**  
Unmet Need



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

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

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

**~\$1.4B** Global  
Gout Market<sup>1</sup>



Expected CAGR of 6.4% from 2022–2029

Krystexxa net sales were ~\$1B in 2023

# PRX-115 Summary

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



### Addressable Market

Approximately 14 million US gout patients, of which ~5% considered to have chronic refractory disease



### Status

Phase I First-in-Human study 8<sup>th</sup> cohort recruitment complete, with follow up ongoing

Phase II planning in progress



### Next Steps

Complete cohort 8 in Phase I study

Phase II study in uncontrolled gout patients anticipated to initiate in 1H 2025



### Asset Overview

- Recombinant PEGylated uricase enzyme produced via ProCellEx<sup>®</sup> plant cell-based expression system
- Favorable safety and 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



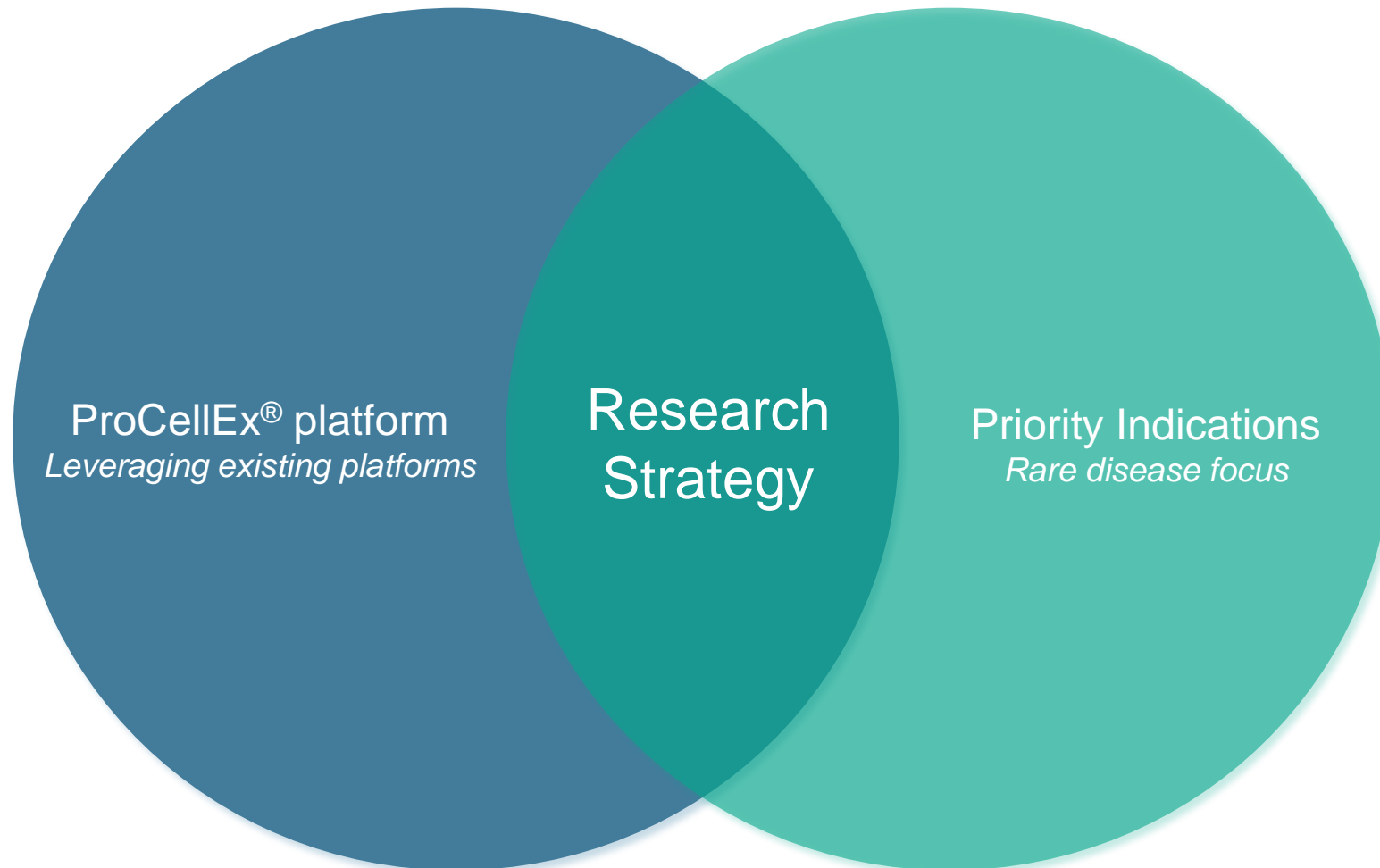
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# Corporate Strategy

# Research Strategy to Fuel Next Stage of Growth

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



# Potential Expansion of ProCellEx® Platform for Drug Delivery

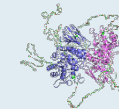
## Exploring platform expansion to include drug delivery modalities for optimized delivery of therapeutic proteins

- 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 / RNAi) in delivery modalities derived from ProCellEx platform (potential collaboration with academic labs)
  - Unlocking additional indications:
    - Specific targeting for delivery to certain organs to address tissue-specific unmet need
    - Blood brain barrier penetration to address CNS disorders
- Initial validation and feasibility studies in progress

## ProCellEx Platform



Protein therapeutics: Plant cell-based expression



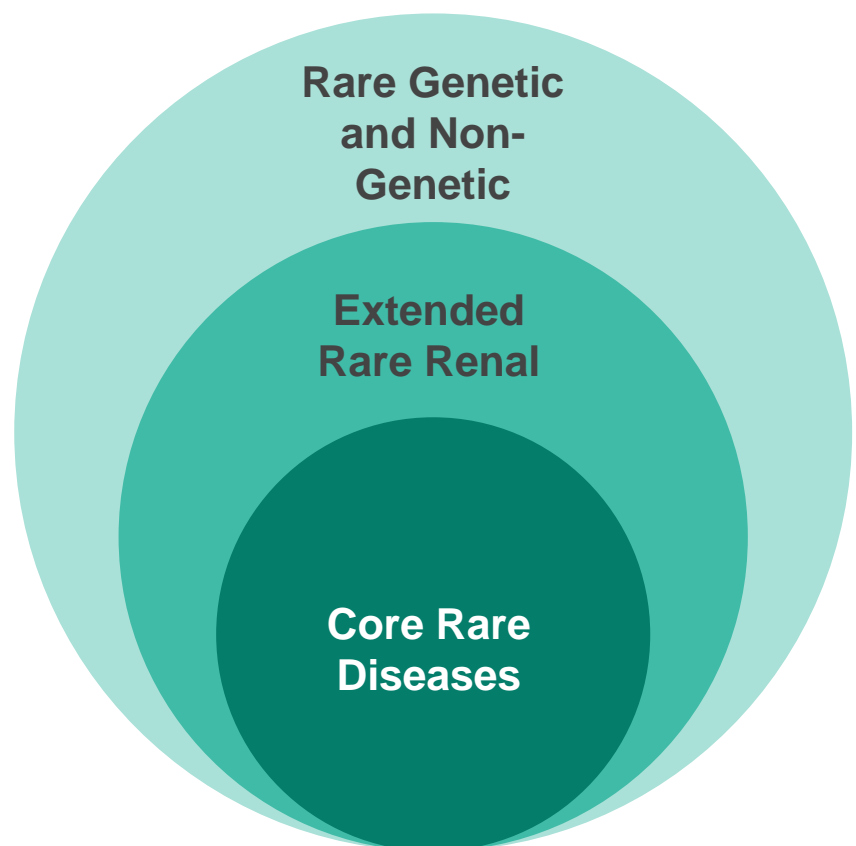
Chemical modification: PEGylation



**Drug delivery: Exploring new modalities**

# Focus on High Unmet Needs in Rare Disease Space

## Focus on 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, MPGN, and others

### Systematic Approach to BD&L

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

# 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

Initial Success

Protalix Now

Next Steps

Vision

**May 2012:**

Protalix's 1<sup>st</sup> approved product

**eleyso**<sup>®</sup>  
(taliglucerase alfa) for injection  
Plant based. People focused.®

**May 2023:**

Protalix's 2<sup>nd</sup> approved product

  
**ELFABRIO**<sup>®</sup>  
(pegunigalsidase alfa-iwxj)

Within 3 years, 4-5 discovery to PhII programs

ProCellEx<sup>®</sup> Platform expansion to include drug delivery modalities

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

# Well Capitalized to Advance Protalix to Next Phase



## CASH

\$48.5M (Q1 2024)



## CASH STREAMS

Three revenue and cash streams from Pfizer, Fiocruz and Chiesi



## CASH RUNWAY<sup>1</sup>

Sufficient cash to support the debt repayment and on-going operations



## EQUITY OPPORTUNITIES

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



## REVENUE

\$3.7M in revenue (Q1 2024)



## NET BURN RATE

Projected: 0 to +\$1.5 M/Q



## DEBT

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



## STRONG PARTNERSHIPS


























Chiesi Farmaceutici S.p.A.  
Pfizer Inc.

Fundação Oswaldo Cruz (Fiocruz)



# Protalix's Evolution: The Last 5 Years

Sharpened focus and increased capital drive the next phase of pipeline development

	2019	2024																				
 <b>Marketed Drugs</b>	Gaucher 	Gaucher  Fabry 																				
 <b>Improved Financials</b>	<ul style="list-style-type: none"> <li>Debt: <b>\$58M</b></li> <li>Cash: <b>\$25M (2Q 2019)</b></li> </ul> 	<ul style="list-style-type: none"> <li>Debt: <b>\$20M → \$0 in Sept'24</b></li> <li>Cash: <b>\$48.5M (1Q 2024)</b></li> </ul> 																				
 <b>Strategic Focus</b>	Based on platform, agnostic	Focus on rare diseases, especially kidney diseases 																				
 <b>Platform Expansion</b>	ProCellEx <sup>®</sup> platform PEGylation 	ProCellEx <sup>®</sup> platform PEGylation Drug delivery modalities 																				
 <b>Pipeline Development</b>	<table border="1"> <thead> <tr> <th>Disc./PreC</th> <th>PhI</th> <th>PhII</th> <th>PhIII</th> <th>Approved</th> </tr> </thead> <tbody> <tr> <td>PRX-115 (Gout)</td> <td></td> <td>PRX-110 (CF)</td> <td></td> <td></td> </tr> </tbody> </table>	Disc./PreC	PhI	PhII	PhIII	Approved	PRX-115 (Gout)		PRX-110 (CF)			<table border="1"> <thead> <tr> <th>Disc./PreC</th> <th>PhI</th> <th>PhII</th> <th>PhIII</th> <th>Approved</th> </tr> </thead> <tbody> <tr> <td>PRX-119 (NET) Lectibody</td> <td>PRX-115 (Gout)</td> <td></td> <td></td> <td> </td> </tr> </tbody> </table>	Disc./PreC	PhI	PhII	PhIII	Approved	PRX-119 (NET) Lectibody	PRX-115 (Gout)			 
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# 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.



**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



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