



PROTALIX
Biotherapeutics

PROTALIX BIOTHERAPEUTICS

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

May 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)



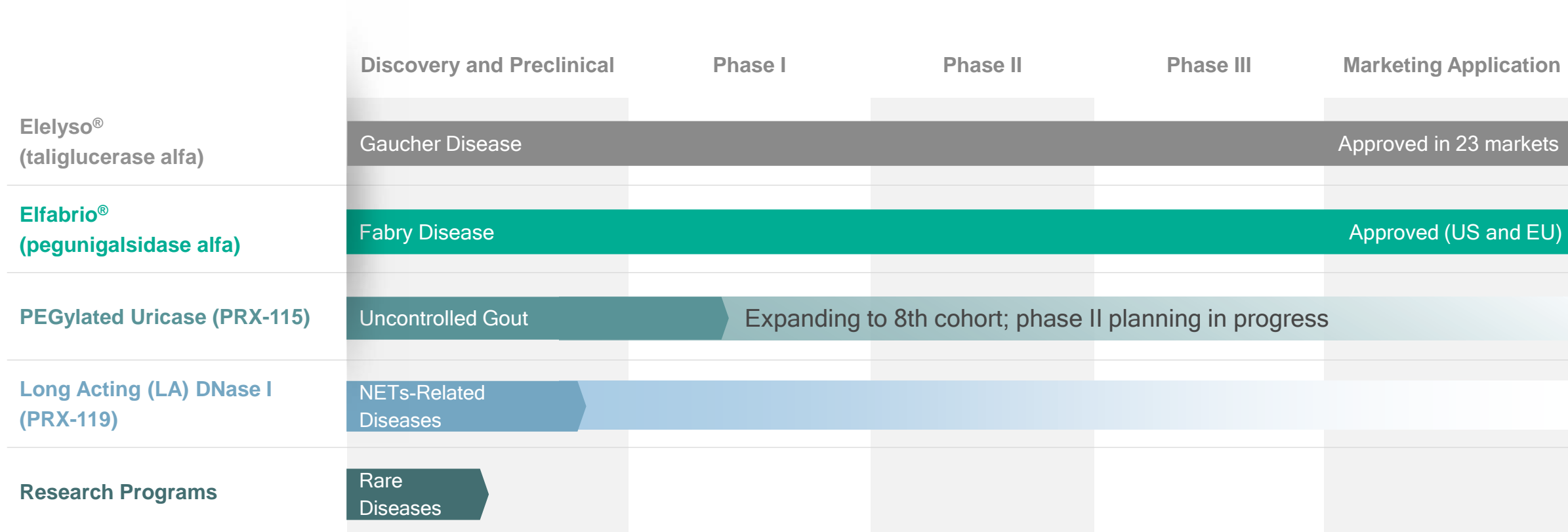
Revenue-Generating

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



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

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** (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



- **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 (Gb₃) 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[®] 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[®] or Fabrazyme^{®1,2})

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 Chiesi³

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 U.S.
3. Based on projected 20-25% share of projected market size increase to ~\$3.1 billion by 2030.

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 (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., E.U. 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
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 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 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-U.S.); 15-40% (U.S.)

Gout



Most Common Inflammatory Arthritis

Gout affects approximately 14 million people in the U.S.

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



Accumulation of Excess Uric Acid

Hyperuricemia leads to deposition of monosodium urate crystals (tophi) in joints, tendons and other tissues

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



Systemic Disease

Gout flares can lead to substantial morbidity, severe pain, reduced quality of life, decreased physical function

Co-morbidities associated with gout include 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[®] ¹

¹ Krystexxa has a "Black Box" safety warning for anaphylaxis and infusion reactions. It is not approved for use in the E.U.

PRX-115 has Significant Potential in Uncontrolled Gout

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

Chronic Refractory
Gout Prevalence



Gout is generally considered severe when urate crystals occur with any of the following:

- Frequent recurrent gout flares
- Chronic gouty arthritis
- Subcutaneous tophi
- Disease elements of gout seen via imaging

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

~\$1.4B Global
Gout Market¹

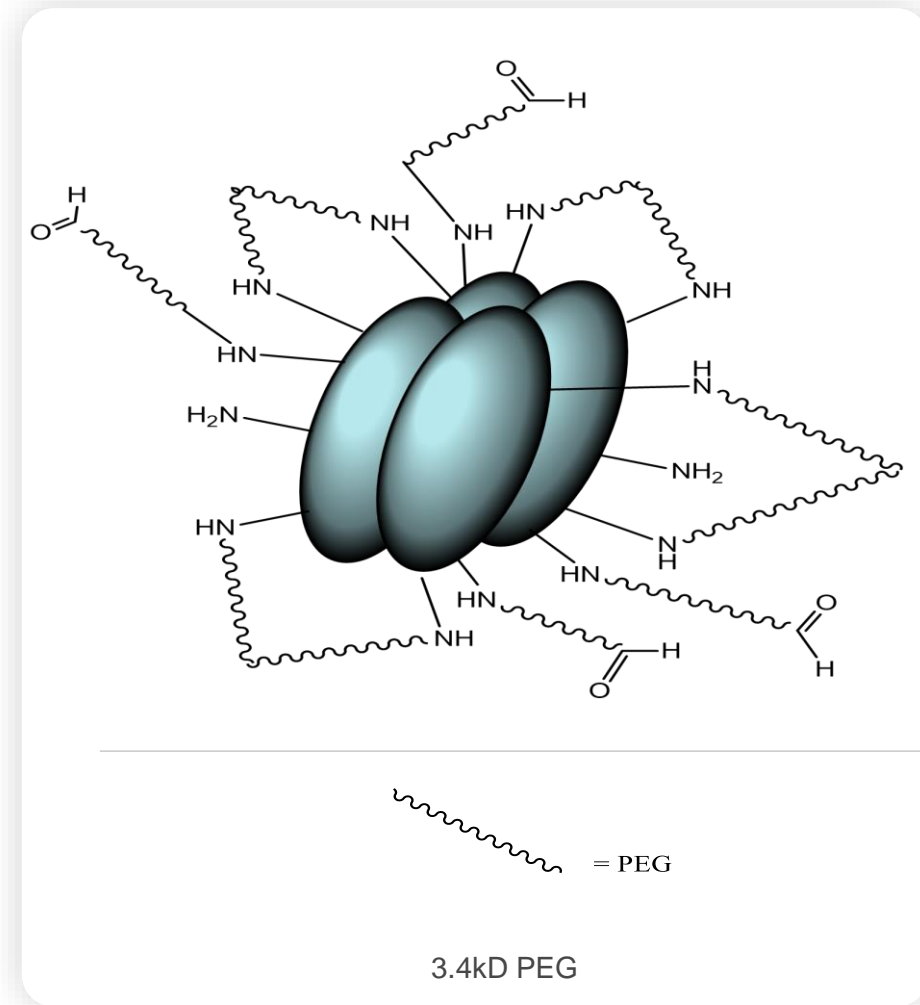


Expected CAGR of 6.4% from 2022-2029

Krystexxa net sales were ~\$1B in 2023

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

- PRX-115 is a PEGylated enzyme designed to potentially have lower immunogenicity 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 Prevent enzyme aggregation and di-sulfide bond formation between the Uricase tetramers.
- The enzyme 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.
- PEGylation potentially reduces immunogenicity by masking immunogenic epitopes, which, together with continued presence, has the potential to induce immune tolerance.



PRX-115 Phase I Single Ascending Dose Study Preliminary Data Summary

First in Human trial enrolled 56 subjects with elevated uric acid levels across 7 dose cohorts

Safety

Favorable tolerability profile

11 of 42 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, which was fully resolved

No other serious AEs were reported

No related AEs were reported in highest dose cohorts 6 and 7

Pharmacokinetics and Pharmacodynamics

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

Reduction of plasma uric acid occurred in dose-dependent manner

PRX-115 exposures increased in dose-dependent manner

PRX-115 Overview

Recombinant PEGylated Uricase Enzyme for Potential Treatment of Uncontrolled Gout



Addressable Market

Approximately 14 million U.S. gout patients



Status

Phase 1 First in Human study expansion to 8th cohort
Phase 2 planning in progress



Next Steps

Enroll and complete cohort 8 in Phase 1 study
Phase 2 study in uncontrolled gout patients anticipated to initiate in H1/25



Asset Overview

- Recombinant PEGylated uricase enzyme produced via ProCellEx 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



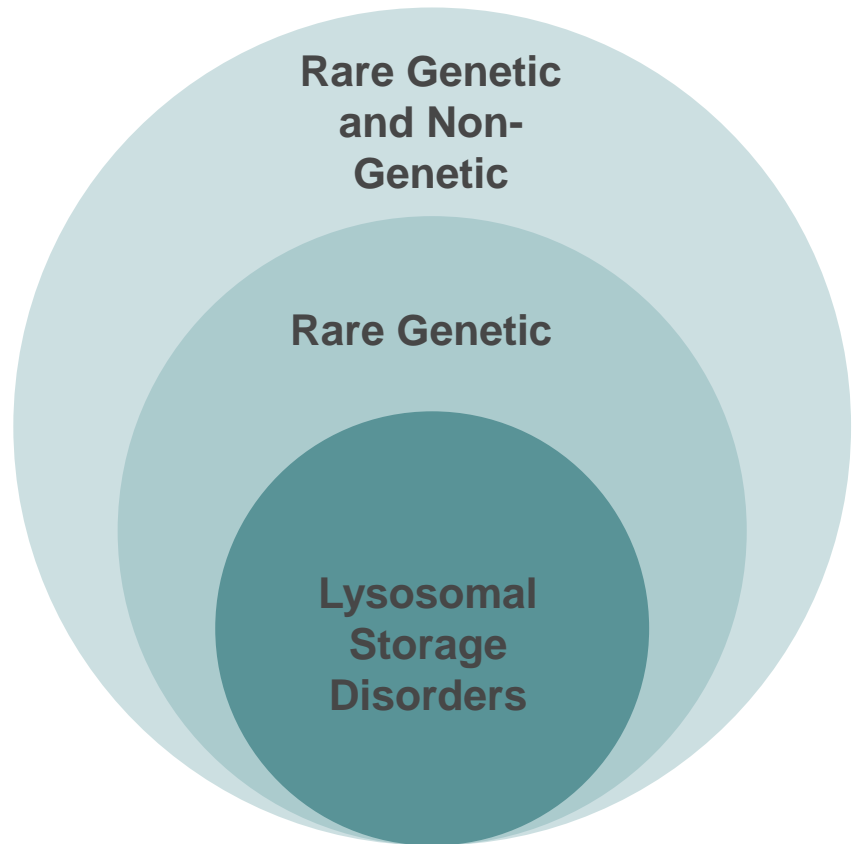
Market Overview

~\$1.4B market for gout overall and growing

Growing Focus on High Unmet Needs in Rare Disease Space

Focus on Rare Disease Space

Goal: *Within 3 years, 4-5 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

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)

Initial Success

Protalix Now

Next Steps

Vision

May 2012:

Protalix's 1st approved product

eleyso[®]
(taliglucerase alfa) for injection
Plant based. People focused.™

May 2023:

Protalix's 2nd approved product

ELFABRIO[®]
(pegunigalsidase alfa-ixxi)

Within 3 years, 4-5 discovery to PhI 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

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⁽¹⁾

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)

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.

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 DEXON 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



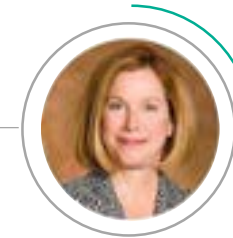
ELIOT FORSTER, PH.D.
Chairman



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

