



PROTALIX
Biotherapeutics

Protalix BioTherapeutics, Inc.

CORPORATE PRESENTATION | **SEPTEMBER 2020**






Note Regarding Forward-Looking Statements

This presentation (the “Presentation”) contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended. The forward-looking statements, including, among others, statements regarding expectations as to regulatory approvals, market opportunity for, and potential sales of, the Company’s product and product candidates, goals as to product candidate development and timing of the Company’s clinical trials, are based on the Company’s current intent, belief and expectations. These statements are not guarantees of future performance and are subject to certain risks and uncertainties that are difficult to predict. Factors that might cause material differences include, among others: failure or delay in the commencement or completion of the Company’s preclinical and clinical trials which may be caused by several factors, including: that the FDA might not grant marketing approval for PRX 102 by the PDUFA date or at all and, if approved, whether PRX 102 will may have significant limitations on its use or be commercially successful; risk that the FDA will request additional data or other conditions of the Biologics License Application (BLA) filing for Accelerated Approval of PRX 102; failure or delay in the commencement or completion of our preclinical 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 monitor patients adequately during or after treatment; and inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; risks associated with the novel coronavirus (COVID-19) outbreak, which may adversely affect our business, preclinical studies and clinical trials; the risk that the results of the clinical trials of the Company’s product candidates will not support the Company’s claims of safety or efficacy, that the Company’s product candidates will not have the desired effects or will be associated with undesirable side effects or other unexpected characteristics; risks related to the Company’s ability to regain compliance with the continued listing standards of the NYSE American and to finance future research and development activities, general and administrative expenses and working capital; risks relating to the Company’s ability to maintain and manage the Company’s relationship with Chiesi Farmaceutici S.p.A. and any other collaborator, distributor or partner; risks related to the Company’s commercialization efforts for alfataliglicerase in Brazil; risks relating to the compliance by Fundação Oswaldo Cruz with its purchase obligations and related milestones under the supply and technology transfer agreement; the risk that despite the FDA’s grant of fast track designation for PRX-102, the Company may not experience a faster development process, review or approval compared to applications considered for approval under conventional FDA procedures; risks related to the FDA’s ability to withdraw the fast track designation at any time; the Company’s dependence on performance by third party providers of services and supplies, including without limitation, clinical trial services; delays in the Company’s preparation and filing of applications for regulatory approval; the inherent risks and uncertainties in developing drug platforms and products of the type the Company is 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, commercially marketed drug for Gaucher disease.  
Fabry Disease	FDA accepted BLA in August 2020 and granted Priority Review for lead asset pegunigalsidase alfa (PRX-102) for the treatment of Fabry disease. In total, the company is conducting three ph:3 trials, which represents the largest Fabry study to date. The ongoing BALANCE trial (ph:3, head to head vs. Fabrazyme) is scheduled for interim results in 1H21; 12 months, for EMA submission.
Partnerships	  
Platform	Proprietary ProCellEx [®] platform for recombinant protein expression and cGMP manufacturing facility successfully inspected and audited by multiple regulatory agencies, including the US FDA and EMA.
Pipeline	(OPRX-106)/Inflammatory Bowel Disease, alidornase alfa (PRX-110)/DNase for multiple indications. Other products in seed and preclinical phases.
Finances	Well capitalized with significant regulatory & commercial milestone (\$1B) & robust royalty opportunities (15-40%).

Note: cGMP = Current Good Manufacturing Practice.



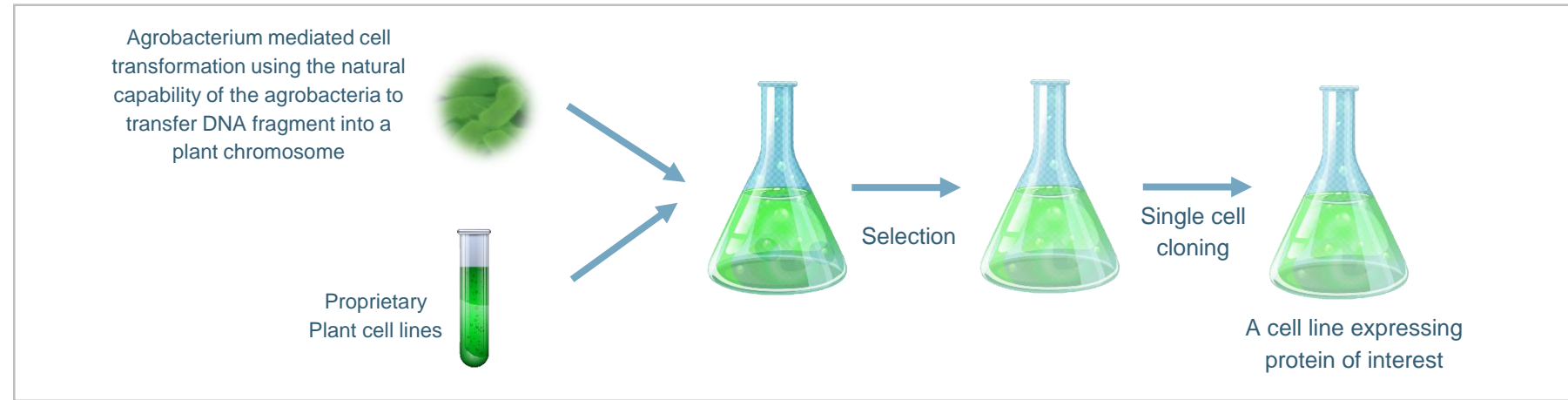
ProCellEx® Platform

First and only company to gain FDA approval of a protein produced through plant cell based expression

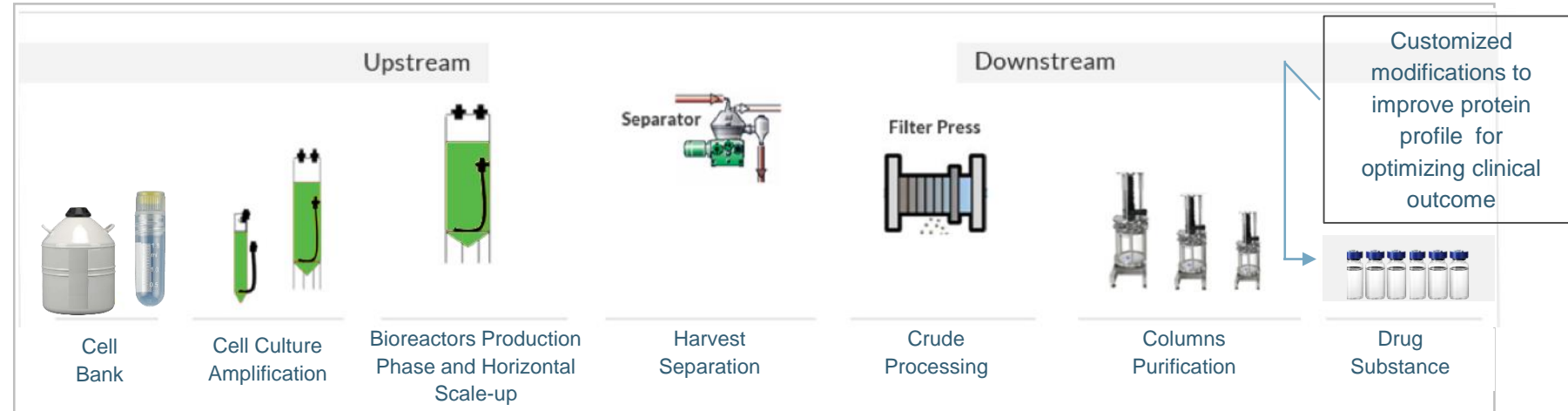


Unique capabilities of tailoring genetic engineering and protein engineering tools for pre/post-production modifications, customized for each individual protein candidate

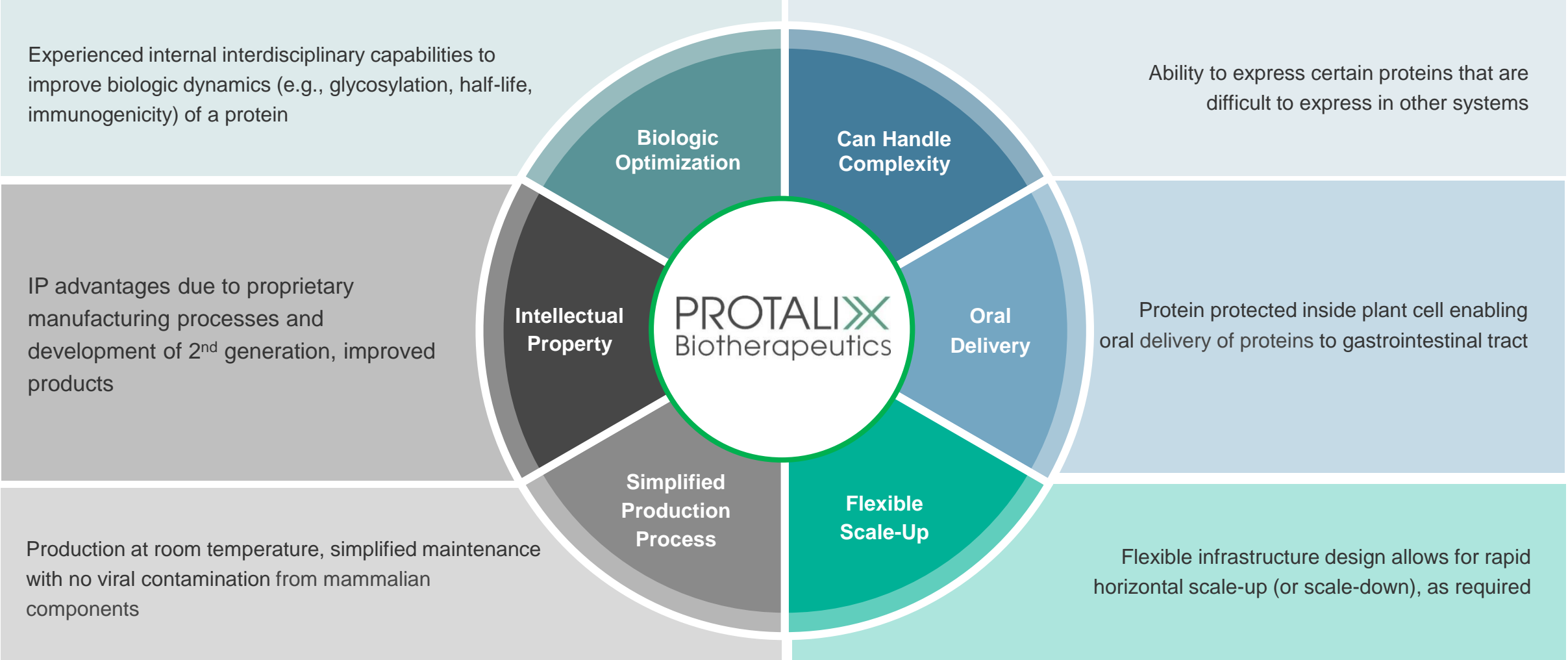
DEVELOPMENT OF TRANSGENIC CELL LINES FOR PRODUCTION OF TARGET PROTEIN



PROCESS OVERVIEW



Advantages of Proprietary Plant Based Platform (ProCellEx®)



Source: Company Information.

Elelyso® for Gaucher Disease

First plant cell derived recombinant protein approved by the

Validation of the ProCellEx® platform

Gaucher disease (go-SHAY) is a rare genetic disorder characterized by the deposition of glucocerebroside in cells of the macrophage-monocyte system. Possible symptoms include enlarged liver and spleen, various bone disorders, easy bruising, and anemia. Left untreated, Gaucher disease can cause permanent body damage and decrease life expectancy.

Elelyso is approved in 23 markets¹. Monetized through a world-wide 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



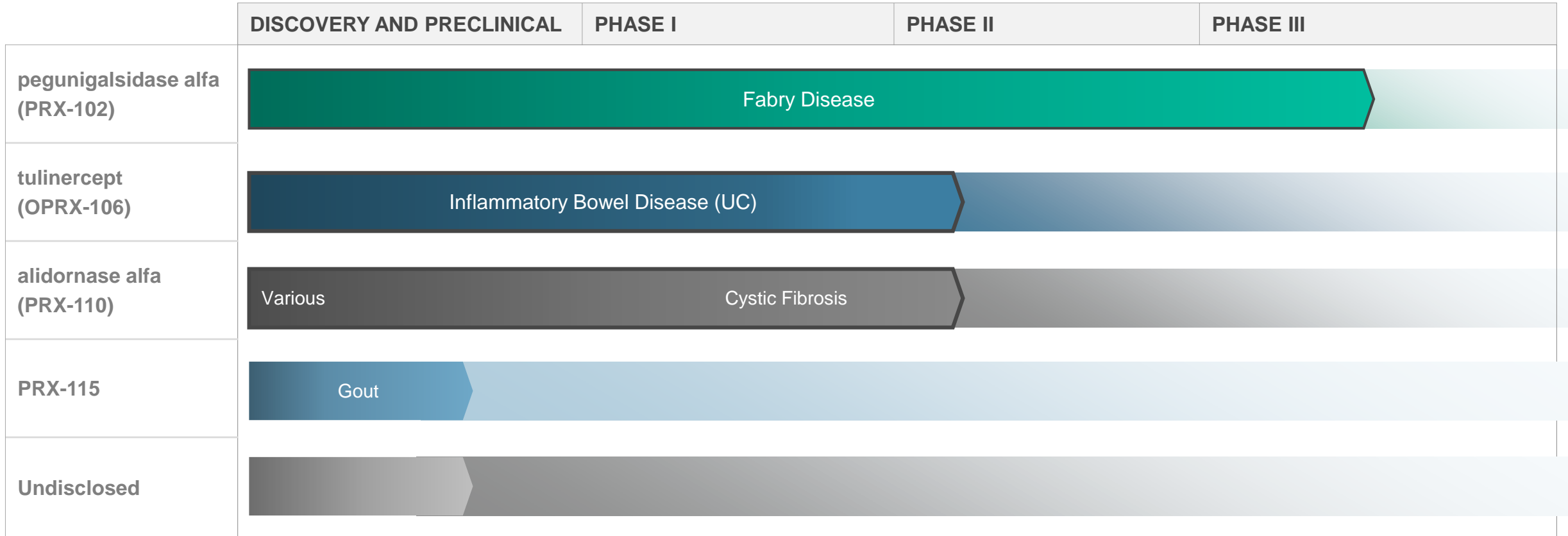
- Sales of ~\$9.1M in Brazil (2019)
- ~27% market share in Brazil
- 10-15% annual growth expected over next 3-5 years



1. Approved in 23 markets including the US, Australia, Canada, Israel, Brazil, Russia and Turkey. 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 ten-year market exclusivity that had been granted to Vpriv® (Shire), which was authorized in August 2010 for the same condition.

Product Pipeline

Recombinant proteins with improved therapeutic profiles that target unmet medical needs and established pharmaceutical markets



All of our pipeline candidates are proteins expressed via our proprietary ProCellEx® system.

Pegunigalsidase alfa (PRX-102) for Fabry Disease

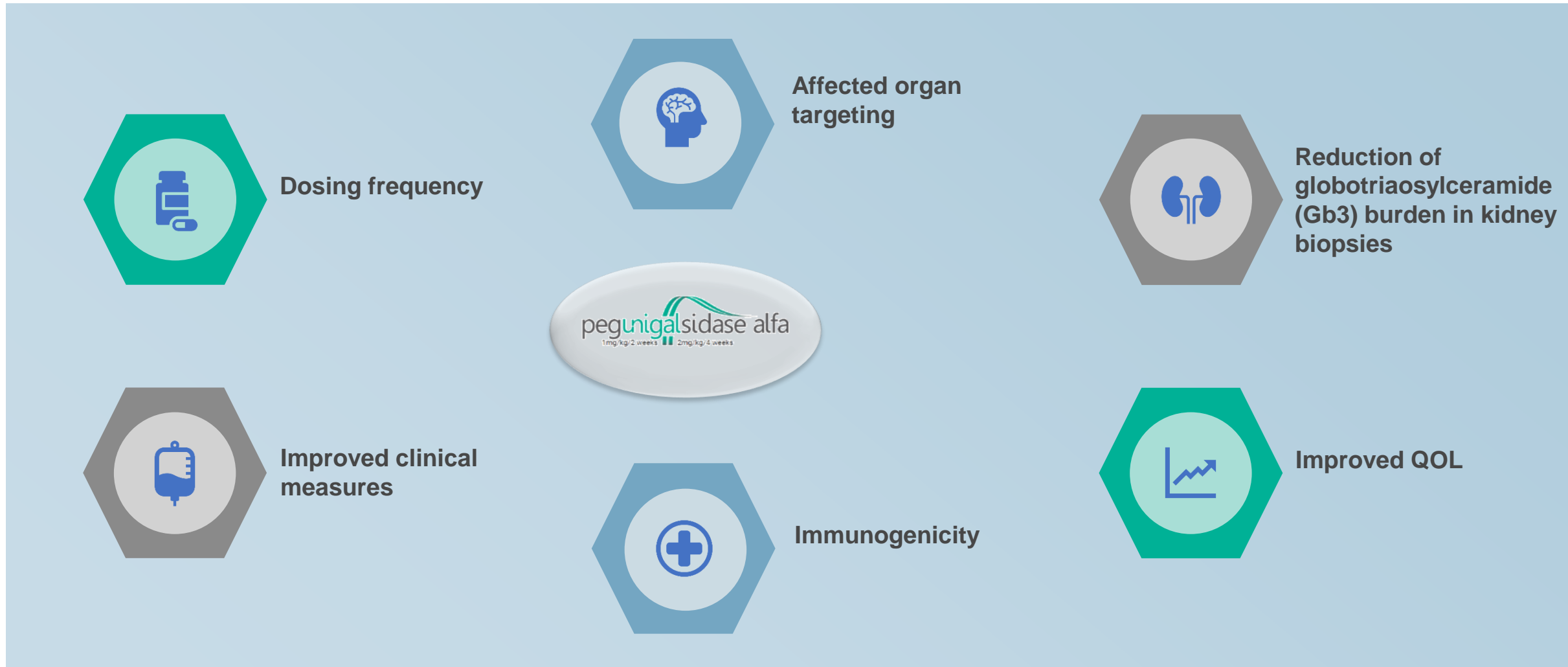
Rare genetic disease
occurs in one of every
40,000 people.

~\$2B+ growing market
(expected CAGR ~10%)

Fabry disease is primarily treated with enzyme replacement therapy (ERT), to replace the missing alpha Galactosidase-A enzyme with a recombinant form of the protein via intravenous infusion 1x every 2 weeks.



Fabry Disease – Treatment Opportunities



Fabry Disease Competitive Landscape

Product Name	Fabrazyme®	Replagal®	Galafold®
Parent Company	Sanofi	Shire	Amicus
Mechanism	ERT	ERT	Pharmacological chaperone
Indication	<p>Fabrazyme is indicated for use in patients with Fabry disease. Fabrazyme reduces GL-3 deposition in capillary endothelium of the kidney and certain other cell types. (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 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 alpha-galactosidase A (alpha-Gal 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	2003 (U.S.); 2001 (E.U.)	Not approved in US ; 2001 (E.U.)	2018 (U.S.); 2016 (E.U.)
Treatment Type	Bi-weekly infusions	Bi-weekly infusions	Oral
Dosing	1mg/kg every 2 weeks	0.2mg/kg every 2 weeks	123 every other day



Pegunigalsidase alfa (PRX-102) for Fabry Disease

pegunigalsidase
alfa (PRX-102)

- Chemically modified plant recombinant alpha-Galactosidase-A designed to provide active and stable enzyme throughout infusion interval for a potentially improved clinical benefit.

Current data have
shown

- Demonstrated significant improvement in renal function following switchover from Replagal with a 5-point improvement in eGFR slope (Bridge Study).
- Circulatory half-life of ~80 hours and active enzyme throughout the infusion interval vs. 2 hours for other ERTs. Targeted enzyme activity in organs affected by Fabry disease.
- Generally well-tolerated to-date; favorable immunogenicity.
- Reduction of globotriaosylceramide (Gb3) burden in kidney biopsies.

Current trials
ongoing in two
dosing and regimens

- Goal of meeting two important unmet needs:
 - Demonstrating potential greater clinical benefit in renal function and other clinical and QOL measures.
 - Lowering the treatment burden of bi-weekly infusions – Improving patient's QOL.



Pegunigalsidase alfa (PRX-102) Clinical Program



1mg / kg 2 weeks Randomized
Double Blind Head-to-Head vs.
Fabrazyme®
24 mos.

78
100% Enrolled

Interim Results – 12 mos. follow up
Expected H1 2021
(Basis for EMA Submission)



1mg / kg 2 weeks Open Label
Switch Over from Replagal®
12 mos.

22
100% Enrolled

Final Results
Expected Q4 2020



2mg / kg 4 weeks Open Label
Switch Over from Fabrazyme®
and Replagal®
12 mos.

30
100% Enrolled

Top Line Results
Expected Q2 2021



Committed Commercial Partner

Global Partnership with Chiesi Farmaceutici S.p.A.

Chiesi's 6,000 employees and \$2B in revenue (2019) provides PLX with the strong Sales & Marketing partner to maximize Unigal's market potential (pending approval) as the centerpiece of their new strategic US based Orphan Drug division



Up to \$1+ billion in potential milestone payments



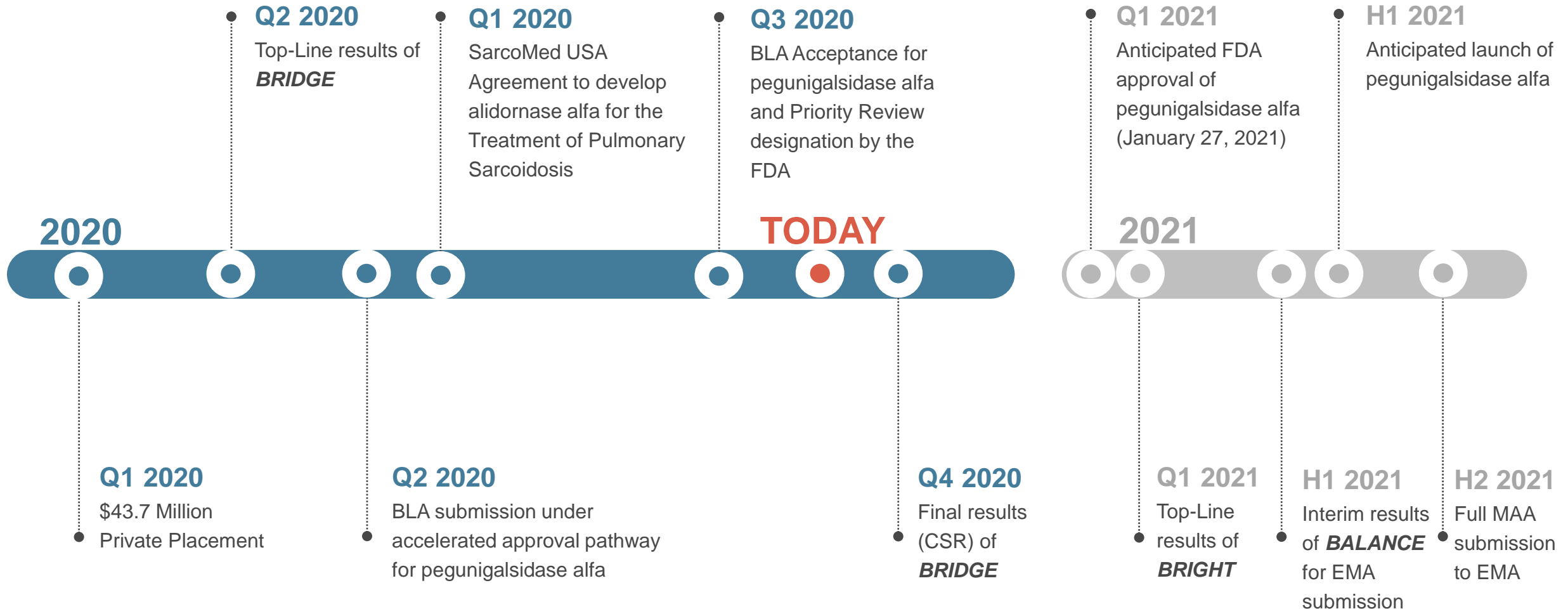
Tiered royalties of 15-35% (ex-US); 15-40% (US)



Committed global partner with a robust sales team and demonstrated expertise in marketing ERTs (while at Genzyme)



Protalix Upcoming Expected Milestones



Tulinercept (OPRX-106) for Inflammatory Bowel Disease (IBD)

Tulinercept is a cutting edge development candidate for IBD expressed via ProCellEx[®] for oral delivery of recombinant proteins whereby the plant cell wall increases resistance and delays to degradation as compared to proteins produced via mammalian cells, and allows for a natural oral administration vehicle.

OVERVIEW

- IBD is a collective reference to autoimmune inflammatory diseases of the gastrointestinal system, causing inflammation and sores on the lining of the digestive tract.
 - Treatment usually begins with anti-inflammatory medications. As the severity of the disease increases, patients are generally treated with tumor necrosis factor (TNF)-alpha inhibitors (anti-TNF), which modulate the immune response.
- The current anti-TNF therapies (infused and injected) are characterized by high immunogenicity and up to a 40% loss of response, most likely due to neutralizing antibodies.
- Anti-TNF alfa biologics currently on the market have “Black Box” safety warnings for malignancies and infections. Similarly, other mechanisms for the treatment of IBD bear serious safety precautions.

OVERVIEW OF CLINICAL TRIALS TO DATE

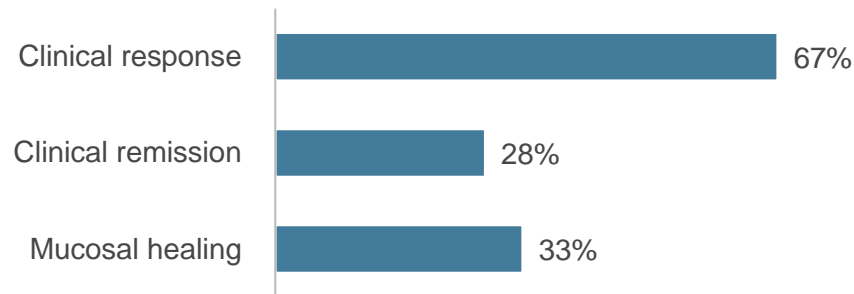
- Two clinical trials of tulinercept were completed for Ulcerative Colitis (UC):
 - **Phase I** – Healthy volunteers: safe and well tolerated.
 - **Phase IIa** – Positive results from 18 UC patients who completed the study⁽¹⁾.
- Two doses explored for induction of remission by week 8.

Sources: Colombel. *Clinical and Translational Gastroenterology*. 2016; Ben Horin. *Alimentary Pharmacology and Therapeutics*. 2011; Remicade, Humira, Simponi, Entyvio, Xeljanz prescribing information. 1. 24 patients were enrolled, 6 patients withdrew, none related to adverse events. Drop out rate consistent with other UC trials reported in similar populations.

Tulinercept (OPRX-106) for IBD

CLINICAL RESULTS FROM PHASE IIA

- 89% of patients experienced improvements in Mayo Score; 72% improved rectal bleeding; 72% improvement in fecal calprotectin and 61% improvement in Geboes score.
- Well tolerated; adverse events (AEs) were mild to moderate and transient.



- No systemic exposure of the drug was detected
- No anti-drug antibodies were detected

Sources: Colombel. *Clinical and Translational Gastroenterology*. 2016; Ben Horin. *Alimentary Pharmacology and Therapeutics*. 2011; Remicade, Humira, Simponi, Entyvio, Xeljanz prescribing information. 1. 24 patients were enrolled, 6 patients withdrew, none related to adverse events. Drop out rate consistent with other UC trials reported in similar populations.

POSITIONING & UPSIDE

- Anti-TNF alfa mechanism – known and established first line treatment for steroid refractory and lack of response to 5-ASA.
- Low likelihood for loss of response due to lack of immunogenicity.
- Local activity in the gut and lack of systemic exposure translates to a better safety profile and removes safety concerns of infections and malignancy which appear in anti-TNF and JAK-inhibitors.
- Oral therapy – convenience in-line with newer innovative therapies.

Alidornase alfa (PRX-110): Actin Inhibition Resistant DNase

OVERVIEW

- Alidornase alfa is a plant cell expressed recombinant human DNase I chemically modified to resist inhibition by actin, thus enhancing enzymatic activity.
- Recombinant human DNase I enzymatically cleaves DNA, yet its activity is inhibited by actin, which is present in the blood.
- In vitro studies have shown that alidornase alfa has a highly improved catalytic efficiency and affinity to DNA, compared to DNase I, even more so in the presence of actin.
- Alidornase alfa was previously tested in Cystic Fibrosis (CF) patients with Phase IIa trial completed in 2018. Alidornase alfa was generally well tolerated in this clinical trial with no serious adverse events reported, and all adverse events that occurred during the study were mild and transient in nature.
- In human sputa samples of CF patients, alidornase alfa exhibits greater activity compared to DNase I, without actin inhibition resistance, in breaking down extracellular DNA and lowering sputum viscosity.

POSITIONING

- Biologically active and safe in humans, alidornase alfa is being developed for other indications where it might have a potential benefit.
- Long acting DNase I is being developed for undisclosed indications.



Well Capitalized with Strong Institutional Shareholder Support

- Recent ~**\$44M** financing (*March 2020*)
- Cash = \$40M (2Q'20)
- \$8.7M in revenue (*H1 20*)
- Cash Runway to 2Q'22
- Burn rate of \$6M/Q, declining as patients shift over to extension study
- \$58M in debt (Convertible Notes) due Nov. 2021
- Strong Institutional shareholder 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.



EINAT BRILL ALMON, PH.D.
SVP, Chief Development Officer

Dr. Almon joined Protalix in December 2004 as a Senior Director and became our Senior Vice President, Product Development. 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, CPA
SVP & CFO

Mr. Rubin has served as our Senior Vice President 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 Senior Vice President, 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 in charge of R&D activities that led to the commercialization of many 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 Vice President 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 MS.c. in Neurobiology, both from the Hebrew University Faculty of Medicine, Jerusalem, Israel.

