Protalix BioTherapeutics
Corporate Presentation

Jefferies Global Healthcare Conference
June 2014

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President & Chief Executive Officer
Note Regarding Forward-Looking Statements

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# Protalix Investment Thesis

## Approved Biologic Drug
- ELELYSO™ approved for commercially treating Gaucher by FDA, Israel MOH, Brazil ANVISA, Chile, Mexico, and other countries. Additional approvals pending

## Strong Commercial Partners
- Collaboration with Pfizer for ELELYSO™ commercialization
- Rights to Israeli and Brazilian market fully owned by Protalix
- Long-term commercial agreement with Brazilian Government

## Attractive Platform
- Plant cell-based protein expression system – ProCellEx®
- Significant advantages over existing expression systems

## Promising Pipeline
- **PRX-102** Fabry disease – IND approved – Phase I/II ongoing
- **PRX-112** Gaucher Oral treatment – Phase I concluded
- **Oral Anti-TNF (PRX-106)** for the treatment of various inflammatory diseases
- **PRX-110** for Cystic Fibrosis
- Protalix retain full rights for ALL pipeline products
## Protalix Pipeline

<table>
<thead>
<tr>
<th>Compound</th>
<th>Indication</th>
<th>Research</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<th>Partner</th>
<th>Market</th>
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<td>PRX-102 (Alpha Galactosidase)</td>
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<tr>
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<td></td>
<td>&gt;$600M</td>
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<tr>
<td>PRX-106 (Oral Anti-TNF fusion)</td>
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<td>&gt;$500M</td>
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<tr>
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<td></td>
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<td>&gt;$600M</td>
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</table>

* Phase I/II study
Key Advantages

• Cost effectiveness and scalability
  ▪ Flexible polyethylene bioreactors, low initial capital investment
  ▪ Rapid, horizontal scalability at low cost in compliance with cGMP
  ▪ Requires less costly “hands-on” maintenance

• Safety and potency
  ▪ Free of any mammalian components
  ▪ No risk of mammalian viral transmission or infection
  ▪ Hundreds of patients have been treated worldwide

• Potentially enables penetration of certain patent protected markets
  ▪ May avoid infringement on method-based patents of other proteins developed with mammalian cell expression systems
ELELYSO for Gaucher Disease
Gaucher Disease
A Genetically Inherited Disorder

Skeletal pathology

Pulmonary hypertension/infiltration

Outcome: Death - Poor quality of life

Source: Beutler and Grabowski, The Metabolic and Molecular Bases of Inherited Disease 2001
Zavesca® (Actelion) is a small molecule drug approved for the treatment of Gaucher disease, however usage is limited due to side effects.

- **Growing Market**
  - Approximately 12,000 patients worldwide
  - Over 6,000 patients are being treated
  - ~50% global market penetration

- **Lucrative Market**
  - Orphan disease supports premium pricing
  - Chronic therapy
  - Concentrated group of prescribers
  - Annual treatment cost is ~$250,000 per year
  - Growing market with estimated annual $1.4 billion of enzyme sales

- **Competition**
  - Cerezyme® (Sanofi-Genzyme) is the major recombinant GCD on the market and is made in mammalian CHO cells
  - VPRIV® (Shire), a recombinant GCD produced in human cancer cells, approved in US and EU

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*Zavesca® (Actelion) is a small molecule drug approved for the treatment of Gaucher disease, however usage is limited due to side effects.*
ELELYSO: Approved Countries

United States

• Priced in the U.S. below the cost of Cerezyme®

• Selected drug of choice by certain regional insurance providers
  • Similar agreements with certain other national and regional providers are currently being discussed

Israel

• Added to the reimbursement national health basket Q1 2013, sales of $5M during 2013.

• Protalix is currently marketing ELELYSO in Israel at a competitive price compared to other products
ELELYSO: Approval Status

Brazil
• Agreement signed in which Brazilian government has committed to purchase UPLYSO from Protalix in return for technology. First shipments to Brazil of drug under the agreement have been made Q1 2014.

Chile
• All adult patients previously treated with other enzyme replacement therapy are now treated with UPLYSO.

Mexico
• Commercial launch has been initiated – March 2014.
• Additional approvals are anticipated in Canada, Australia, Argentina and other Latin American countries throughout 2014.
Terms

• Pfizer and Protalix share net profit and net loss of ELELYSO on a 60% / 40% basis. Only certain limited capped expenses allowed

Territories

• Pfizer retains exclusive worldwide rights outside of Israel and Brazil
• Protalix retains exclusive commercialization rights in Israel and in Brazil

Manufacturing

• Protalix manufactures ELELYSO Drug Substance

Oral Gaucher treatment

• Protalix retains full global rights to oral GCD program
• ~650 patients treated, additional untreated patients

• Enzyme therapy is fully paid for by the Brazilian Ministry of Health

• Brazilian Minister of Health, Dr. Alexander Padilha and his senior team visited Protalix’s facility
Protalix and Brazil’s Ministry of Health enter into supply and technology transfer agreement for UPLYSO (Marketing name in Brazil)

Fiocruz (an arm of the Brazilian Ministry of Health) is required to complete purchase of at least ~$280 million worth of UPLYSO to reach the final stage of the transfer of Protalix technology

Fiocruz is committed to purchase ~$40M of UPLYSO over the first 2 years

Each subsequent year a minimum purchase of ~$40M of UPLYSO is required or Protalix has the right to terminate the agreement

Fiocruz is obligated to purchase ~$280M of UPLYSO before Protalix is obligated to complete the technology transfer
Financial Benefits

- Creates partnership with one of world’s growing economies
- Lucrative economics and steady cash flow for Protalix
- Ability to generate visible, meaningful revenues on limited operational expenses
- Relatively short penetration period into the market
- Eliminates the need to participate in bids
- Secures prices over a long period

Drug Supply / Technology Transfer Description

- Throughout the entire agreement, Fiocruz and MOH will support and distribute UPLYSO in Brazil
- Upon completing all four stages which include performing a clinical study, Fiocruz will be able to produce UPLYSO for the Brazil market on its own
- After the technology transfer is complete, Protalix will receive mid-single digit royalties on net sales by Fiocruz
UPLYSO Fiocruz Label in Brazil
First Shipment made under Agreement

UPLYSO* alfataliglycerase
(200 unidades)

Fabricado por:
Wasserburger Arzneimittelwerk GmbH
Wasserburg – Alemanha

Embala por:
Pharmacia & Upjohn Co.
Kalamazoo, Michigan – EUA

Registrado por:
LABORATÓRIOS PFIZER LTDA.
Av. Presidente Tancredo de Almeida Neves, 1336
CEP 07112-970 – Guarulhos - SP
CNPJ nº 46.070.386/0001-89
www.pfizer.com.br

Importado por:
Fundação Oswaldo Cruz
Instituto de Tecnologia em Imunobiológicos –
Bio Atéquinos
RJ – Brasil – CEP 21040-990
CNPJ nº 33.761.355/0001-35
Frm. Resp.: José Cláudio Gumerad
CRF-SP nº 42746

Composição: cada frasco-ampola de Uplyso* contém 200 unidades de alfataliglycerase. MA – 1.0216.0229.001-3

Conservar o medicamento sob refrigeração (entre 7 e 8°C), protegido da luz. Não congelar.
Cuidados após reconstituição e diluição: vide baixa.
Mantenha o medicamento em sua embalagem original.
Informações ao profissional da saúde, indicações, contraindicações e precauções: vide baixa.

* Marca depositada

USO SOB PRESCRIÇÃO MÉDICA

SAUDE NAO TEM PREÇO

SAC 0800-7701575

USO SOB PRESCRIÇÃO MÉDICA

QUALIDADE
Pfizer

RASPE AQUI COM UMA MOEDA

TODO MEDICAMENTO DEVE SER MANTIDO FORA DO ALCANCE DAS CRIANÇAS.
PRX-102 for Fabry Disease - A modified “Bio Better” Enzyme
Fabry Disease

Accumulation of Gb3 (α-Galactosidase-A substrate) in lysosomes

Hypertension and cardiomyopathy

Increased risk of stroke

Renal insufficiency and renal failure

Outcome: Poor quality of life - Death

Source: Adopted from Najafian et al., Kidney Int. 2011
The chemical modification:
- Both protein sub-units are PEGylated, resulting in a covalently bound active and stable dimer

Advantages:
- Improved stability
- Longer circulatory half life
- Enhanced uptake and activity in target organs

PRX-102 properties can potentially lead to:
- Better clinical efficacy
- Lower dosing
- Longer intervals
Currently available treatment:

- Fabrazyme® (Genzyme) and Replagal® (Shire) - Not approved in the U.S.
- Both mimic the natural non-covalently bound homo-dimer
- Marketed products' half-life is a few minutes long
- Not all clinical parameters sufficiently addressed

Protalix approach:

Objective:
- Develop a Bio-Better enzyme with superior clinical effect

Method:
- Generation of a stable dimer via covalent cross-linking
Enhanced Circulatory Half-life

Half-life ($t_{1/2}$)
Commercial - 13 min
PRX-102 - 581 min
PRX-102: Potential Best-in-Class Fabry Treatment

Improved In-vivo Activity: PRX-102 vs. Replagal

Single injection of either PRX-102 or Replagal®

Heart

Kidney

PRX-102 exhibits higher activity levels in target organs over time in Fabry mice after a single injection
PRX-102 Clinical Plan Outline

Phase I/II:

- 18 patients (6/group), IV infusion once every two weeks
- 3 doses (0.2mg/Kg, 1 mg/Kg, 2 mg/Kg)
- Duration – 12 weeks (7 infusions, 3 months)

Extension study:

- 18 patients, IV infusion once every two weeks, at same doses as in Phase I/II
- Duration Total – 38 weeks (20 infusions, 9 months)

Study evaluation

- Skin and kidney biopsies + cardiac MRI (after 6 months)
PRX-102 Clinical Development Status

- Ongoing phase I/II trial in 18 Fabry patients under IND from FDA
- Patients currently being treated and/or recruited in sites in the United States, South America, Europe and Australia
- Recruitment to be completed in H2 2014
- Report interim results in H2 2014
- Final study report expected H1 2015
- Phase III – expected 2015
Protein Oral Delivery

• Oral delivery of therapeutic proteins
  • Long time goal of the biopharmaceutical industry
  • Currently only very limited success

• The plant cell advantage
  • The concept: plant cell wall (cellulose) serves as protective agent against the gastric environment and can serve as an oral administration vehicle
Schematic Plant Cell
Edible carrot cells expressing recombinant human glucocerebrosidase (prGCD)

Produced by the same cells as the approved drug taliglucerase alfa

Carrot cells contain “ready to use” enzyme

Once in blood, enzyme is expected to act like IV administered taliglucerase alfa

PRX-112 carrot cells are prepared as “patient friendly” oral formula
Biodistribution of Active prGCD Following Oral Administration

prGCD in pig plasma

prGCD in rat plasma

prGCD in rat target organs

GCD activity mg/gr tissue

Control (-)  (-) prGCD
An exploratory, open-label study to evaluate the safety of PRX-112 and pharmacokinetics of oral prGCD (plant recombinant human glucocerebrosidase) in Gaucher patients

**Design**
- Adult Gaucher patients
- Three dose groups
- PRX-112 cell suspension administered orally as follows:
  - **Treatment Period A:** Single administration followed by PK
  - **Treatment Period B:** Three consecutive daily administrations followed by PK after last dosing

**Primary Objective:**
- To evaluate the safety of oral PRX-112 in Gaucher patients

**Secondary Objective:**
- Evaluate the pharmacokinetics (PK) of orally administered prGCD (plant recombinant human glucocerebrosidase).
Patient Population

Main Inclusion Criteria

- Males and females, 18 years or older.
- Confirmed Gaucher disease by low leukocyte GCD activity level
- Platelets count < 100,000 mm$^3$ (last 4 pts.)

Main Exclusion Criteria

- Presence of any GIT disease or symptomatology
- Subjects with any history of allergic response to drugs or other allergies
- Subjects who donated blood in the last three months, or received blood or plasma derivatives in the last six months

Demographic

<table>
<thead>
<tr>
<th>Demographic</th>
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<tbody>
<tr>
<td>Age</td>
<td>19.2-76.9</td>
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<tr>
<td>Gender</td>
<td>62.5% males 37.5% females</td>
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</tbody>
</table>
Phase I Results - Safety

- Drug was well tolerated
- No drug related serious adverse reactions reported
- No patient discontinued the study prematurely
- No treatment induced antibodies
Results: GCD Activity in Leukocytes Following Orally Delivered prGCD
PK Summary of Oral Delivered prGCD

- Active enzyme was detected in patients' blood circulation following oral administration.

- The observed increase in Cmax and the AUC values of active GCD in leukocytes constitute evidence of absorption of prGCD after oral administration of PRX-112.

- PK profile is different than IV administered ERT, continuous secretion over ~30h vs. minutes.
# Effect of Oral prGCD on Thrombocytopenia

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Gender</th>
<th>Dose (U)</th>
<th>Platelet levels baseline (10^3/ml)</th>
<th>Platelet levels end of study (10^3/ml)</th>
<th>Change in plt level</th>
<th>% change in plt levels</th>
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<tbody>
<tr>
<td>A01-001</td>
<td>M</td>
<td>~250</td>
<td>60,000</td>
<td>61,000</td>
<td>1,000</td>
<td>1.67</td>
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<tr>
<td>A01-002</td>
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<td>95,000</td>
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<td>56,000</td>
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<td>-1.75</td>
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Platelet levels in 3/8 thrombocytopenic patients showed meaningful increase after treatment with oral GCD.
Overall Conclusions

- Presence of an active enzyme was detected in patients' blood circulation following oral administration.
- Oral GCD was found to be safe and well tolerated in all 16 patients across all of the three doses tested.
- Some of the patients with thrombocytopenia demonstrated an unexpected meaningful improvement in platelet count.
Clinical Development Plan

- **Phase 2a** – 28-day Dose-Response PK and Safety study performed in 10 naïve adult Gaucher patients

- **Phase 2b** – 6-month clinical study, to be performed in 12 naïve adult Gaucher patients demonstrating defined diseases parameters

- **Phase 3** – Switch over, 12-month clinical study expected to be performed in patients on a stable ERT regimen with any enzyme, switching them to PRX-112
Oral PRX-106 - Oral administration of plant anti-TNF fusion protein for the treatment of inflammatory indications
Oral Administration of Plant Cells Expressing Anti-TNF Fusion Protein (PRX-106) for the Treatment of Colitis
Oral Administration of Plant Cells Expressing Anti-TNF Fusion Protein (PRX-106) for the Treatment of Colitis
Orally Administered Plant Cell-Expressed Anti-TNF Fusion Protein (PRX-106) Alleviates Immune-mediated Colitis

* p<0.02

weight loss (%)
Orally Administered Plant Cell-Expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Reduces IFNγ serum levels

Oral PRX-106 reduced serum inflammation marker IFNγ
Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Promotes Serum Levels of Anti-Inflammatory IL-10
Orally Administered Plant Cell-Expressing PRX-106 reduces the severity of DSS-induced colitis
Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) For Diabetes, Hyperlipidemia and Fatty Liver Disease

Phase I clinical study planned for 2014
Oral PRX-106 Anti-TNF Summary

Positive results from Hepatitis (Con-A) model:
- Two consecutive experiments
- Oral PRX-106 reduced inflammation
- Oral PRX-106 reduced necrosis in the liver

- Colitis -TNBS model
- Colitis -DSS model

Ongoing experiments in other models:
- Fatty liver (High fat diet model)

- Phase I clinical study planned for 2014
Financial Overview

• ~ 93.5M shares outstanding (31.3.2014)

• US, Israeli and EU institutional holders

• Publicly traded on NYSE MKT and TASE

• $69M convertible note due by Sept. 2018

• 10 years of tax exemption after using NOL (currently ~ $100M)
## Financial Status

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<th>Quarter ended 3/31/2014</th>
<th>Year ended 12/31/2013</th>
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<td>Cash &amp; Cash Equivalents</td>
<td>$77.7</td>
<td>$86.4</td>
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<td>Total Revenues</td>
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<td>R&amp;D Expenses, net</td>
<td>6.1</td>
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<td>SG&amp;A Expenses</td>
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<td>Net Loss</td>
<td>$7.3</td>
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$ in millions
Commercial Milestones for 2014

• In Israel, treat approximately 25% of adult Gaucher patients with ELELYSO

• In Brazil, invoice approximately ~$40 million through July 31, 2015 in accordance with the technology transfer and supply agreement

• Maintain profitability and growth in collaboration with Pfizer with Protalix’ share continually increasing

• Potential to sign agreements with regional and national insurance providers in the United States

• Anticipated marketing approvals for ELELYSO/UPLYSO in Canada, Australia and Argentina
Upcoming Clinical Milestones

Oral GCD

• Perform phase II clinical trial in 2014

PRX-102

• Complete recruitment for phase I/II clinical trial in 2H 2014; report interim data in 2H 2014 and full results in 1H 2015, Phase III - expected 2H 2015

PRX-106 (oral anti-TNF)

• Initiate phase I clinical trial for the treatment of autoimmune diseases in 2014

PRX-110

• File IND enabling the initiation of phase I clinical trial in Cystic Fibrosis in 2014