PROTALIX Biotherapeutics

Analyst Event

Thursday, June 20, 2013

The Westin New York Grand Central Hotel

New York, NY

Note Regarding Forward-Looking Statements

The presentations set forth herein contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, 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 the Company's product candidates, goals as to product candidate development and timing of our 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. Actual results may differ materially from these forward-looking statements because of the Company's unproven business model, its dependence on new technologies, the uncertainty and timing of clinical trials, the Company's ability to develop and commercialize products, its dependence on collaborators for services and revenue, its substantial indebtedness and lease obligations, its changing requirements and costs associated with planned facilities, intense competition, the uncertainty of patent and intellectual property protection, dependence on key management and key suppliers, the uncertainty of regulation of products, the impact of future alliances or transactions and other risks described in the Company's filings with the 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.

Agenda & Speakers

Supply and Technology Transfer Agreement in Brazil
Dr. David Aviezer, President and CEO, Protalix Biotherapeutics

Commercial Update on Elelyso / Uplyso for Gaucher Disease
Vera Wu, Global Asset Lead, Elelyso/Uplyso, Pfizer

PRX-102 for Fabry Disease
Dr. Gregory Pastores, Associate Professor, Neurology and Pediatrics, NYU School of Medicine
Dr. Einat Almon, Senior Vice President, Product Development, Protalix Biotherapeutics

Oral GCD for Gaucher Disease
Dr. Yoseph Shaaltiel, Executive Vice President, Research and Development, Protalix Biotherapeutics
Prof. Ari Zimran, Director, Gaucher Clinic, Shaare Zedek Medical Center, Jerusalem

Preclinical Pipeline Candidates PRX-106, PRX-110 & PRX-107
Prof. Yaron Ilan, Director, Department of Medicine, Hebrew University Hadassah Medical Center
Dr. Yoseph Shaaltiel, Executive Vice President, Research and Development, Protalix Biotherapeutics

Q&A Session

Supply and Technology Transfer Agreement in Brazil

Dr. David Aviezer, President and CEO, Protalix Biotherapeutics

Gaucher Market in Brazil

- ~600 patients treated
- ~US$65M market per year
- Additional untreated patients
- Enzyme therapy is fully paid for by the Brazilian Ministry of Health
- Currently two enzymes are available:
  - Cerezyme
  - Uplyso

Supply and Technology Transfer: Deal Description

Stage 1

- Protalix sells fully packaged vials to Fiocruz

Stage 2

- Protalix sells naked vials to Fiocruz which will be labeled and packed in Brazil
- Fiocruz set-ups and gets approval for a fill and finish facility

Stage 3

- Protalix sells drug substance to Fiocruz, which they will lyophilize, label and package into vials
- Fiocruz builds a validated manufacturing facility for UPLYSO

Stage 4

- Protalix establishes cell technology for Uplyso in Brazil
- Fiocruz conducts clinical trials with drug produced in their facility
- Fiocruz applies for approval of the facility and drug with ANVISA
- Protalix establishes cell bank for Uplyso in Brazil

Deal Description Cont…

- Throughout the entire agreement, Fiocruz will support and distribute Uplyso in Brazil
- Upon completing all four stages, 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

Deal Terms

- Initial term is 7 years – can be extended by an additional 5 years
- 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
- The price per vial under the agreement is similar to the current market price in Brazil
- Fiocruz is financially responsible for costs incurred by Protalix in conjunction with the technology transfer process

Financial Benefits of the Deal

- Creates partnership with one of worlds 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

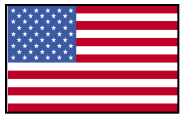
Commercial Update on Elelyso / Uplyso for Gaucher Disease

Vera Wu, Global Asset Lead, Elelyso/Uplyso, Pfizer

Elelyso / Uplyso Update

elelyso™
(taliglucerase alfa) for injection
Plant based. People focused.™

uplyso™
taliglucerasa alfa



U.S.

Mexico

Brazil

Chile

elelyso™
(taliglucerase alfa) for injection
uplyso™
taliglucerasa alfa

Fabry disease

Diagnosis and Management

Gregory M. Pastores, MD

NYU School of Medicine

New York, NY

Fabry Disease

Angiokeratoma corporis diffusum

Johann Fabry (Germany)

1860-1930

Family H

Three men and one woman are known to have been affected by angiokeratoma corporis diffusum in this family (Fig. 4). The mother of one patient (Case 19)

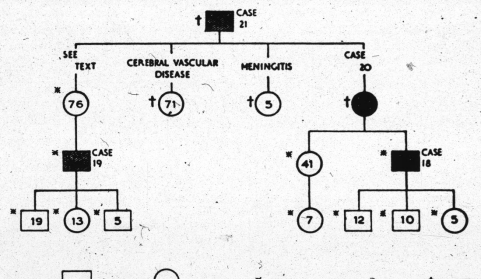


FIG. 4. Family H. The ages are given of individuals believed to be unaffected.

is alive and active at the age of 76; her blood-pressure is 170/90, and she has slight proteinuria. An electrocardiogram shows left ventricular hypertrophy, and the blood urea is 41 mg. per 100 ml. The family has been previously reported in parts by Anderson (1898), Wallace (1958), and Colley, Miller, Hutt, Wallace, and de Wardener (1958).

Arch. Dermatol. Syph. 43:187, 1898

Ein Beitrag zur Kenntniss der Purpura haemorrhagica nodularis (Purpura papulosa haemorrhagica Hebrae).

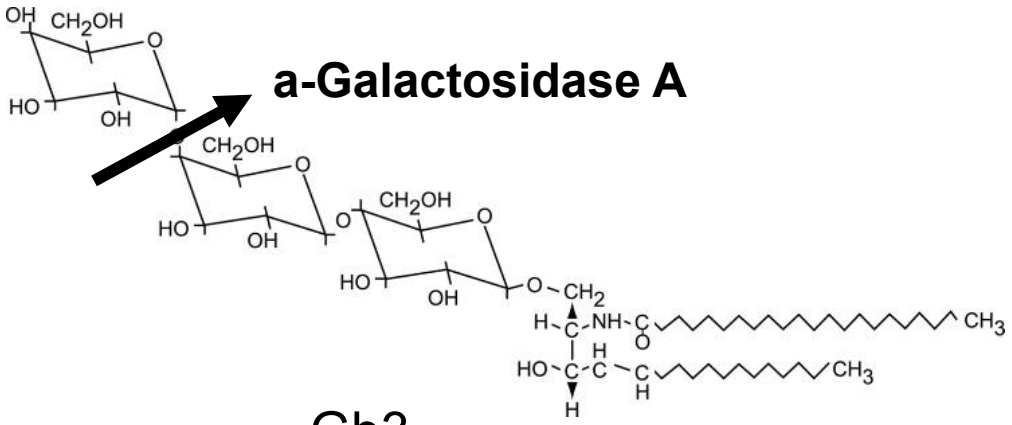
Von

Dr. med. **Joh. Fabry** in Dortmund.

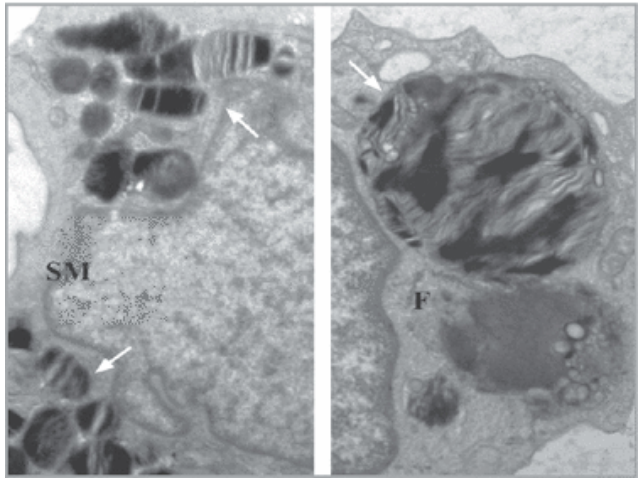
(Hierzu Tafel VII—X.)

Fabry disease

Alpha-Galactosidase deficiency

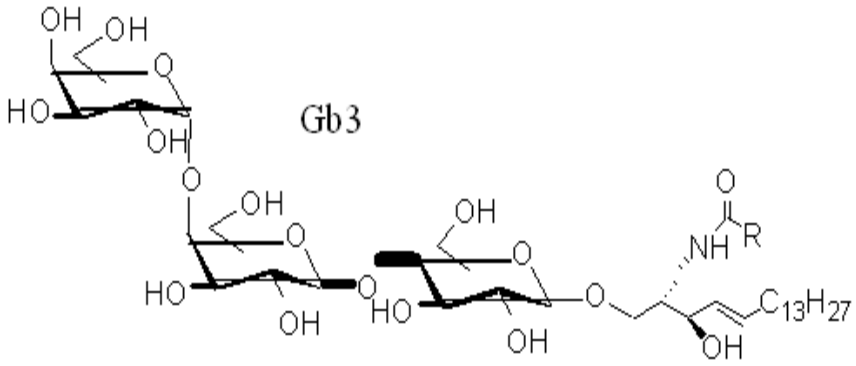


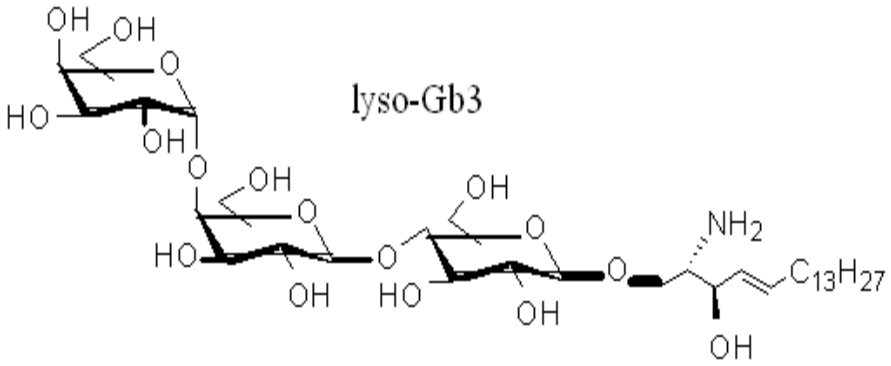
Gb3

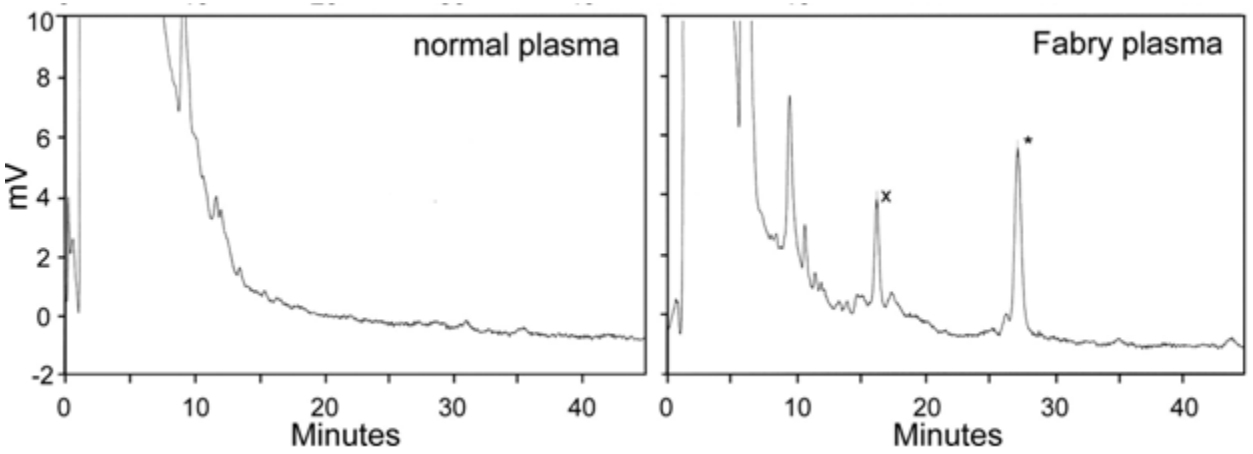


- Zebra bodies found in several types of cells: endothelial cells, pericytes, macrophages, fibroblasts, sweat gland cells, smooth muscle cells, glomerular epithelial cells, neuronal cells

Lyso-Gb3



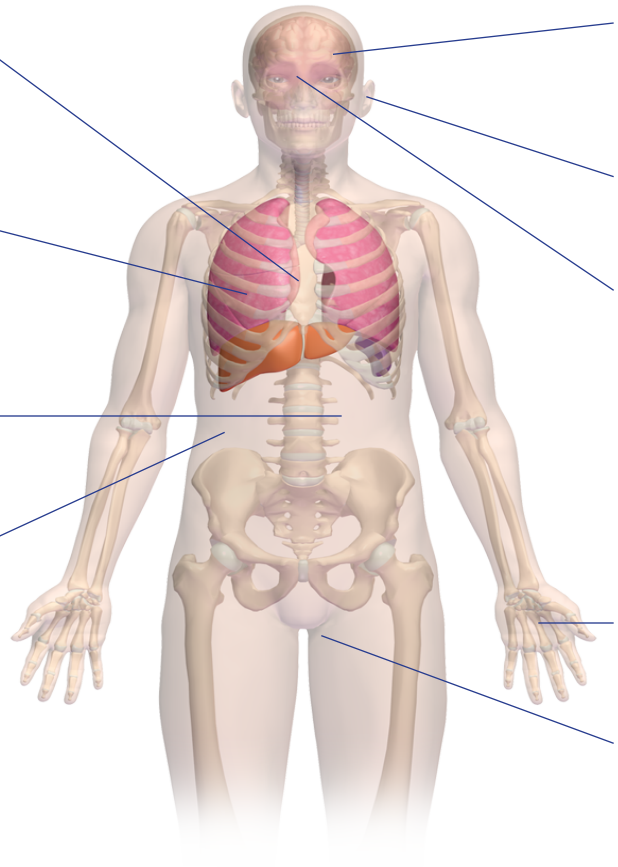




Aerts JM, et al. Proc Natl Acad Sci U S A. 105(8):2812,2008

Fabry disease:

Clinical expression



Cardiomyopathy
Arthytmia

Obstructive
airway disease

Gastrointestinal
problems

Renal
insufficiency

Cerebrovascular events:
TIA, Stroke

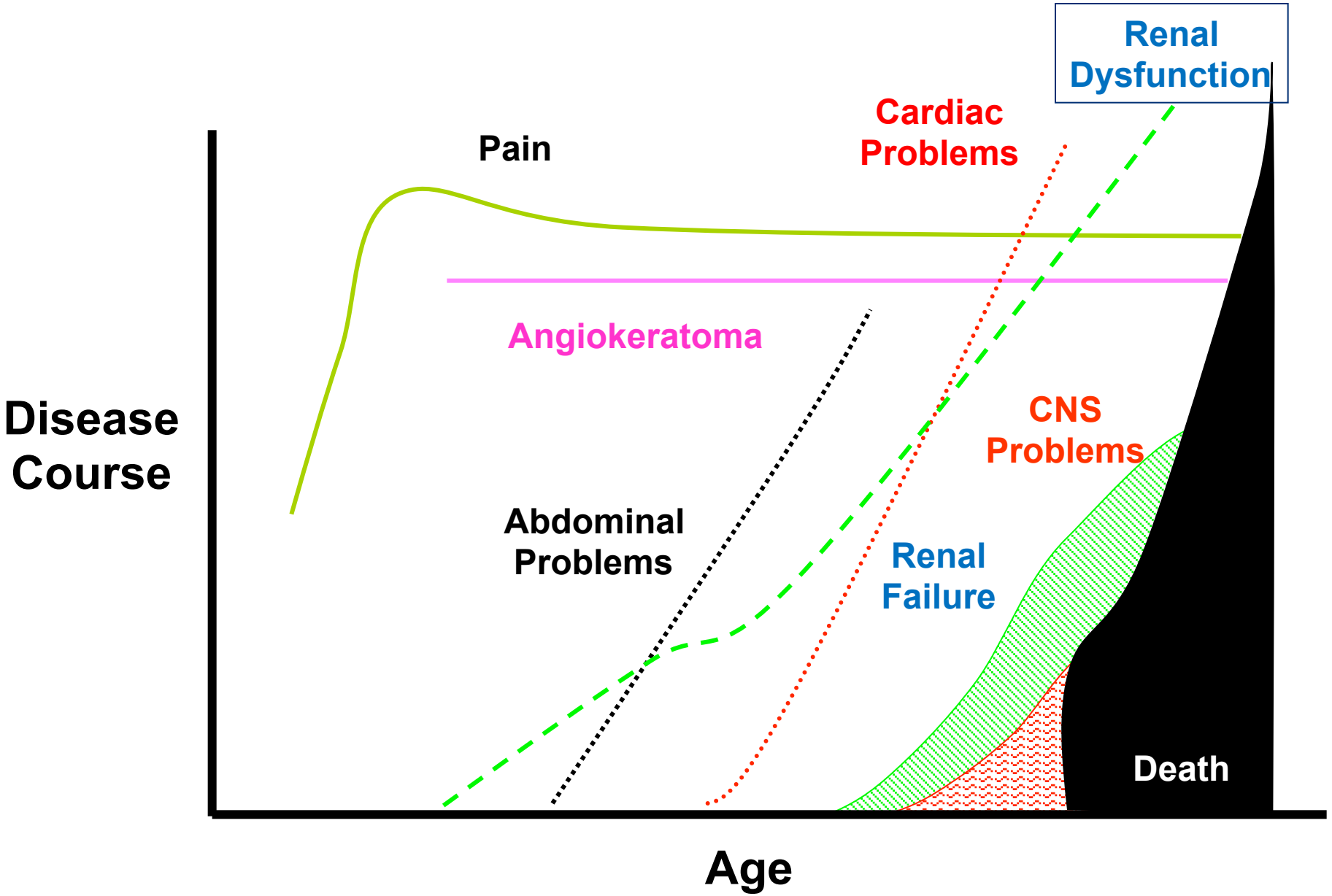
Hearing loss

Cornea Verticillata

Acroparesthesia

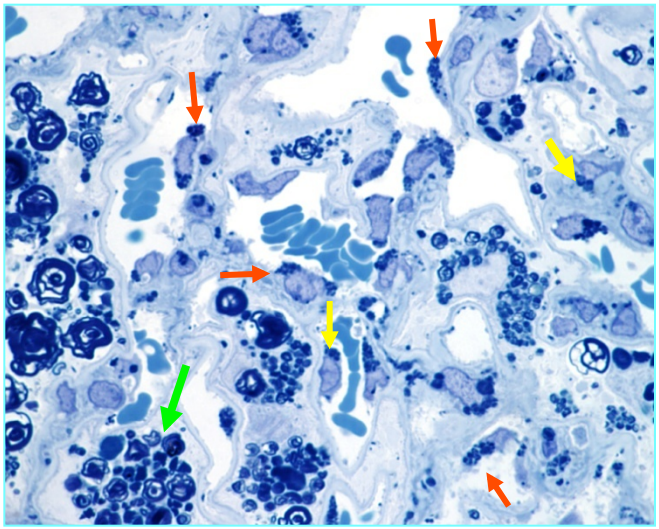
Angiokeratoma

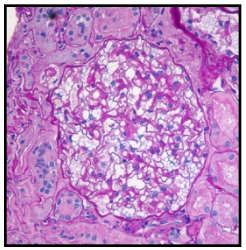
Fabry disease: Clinical course

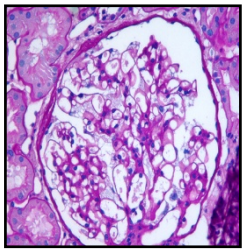


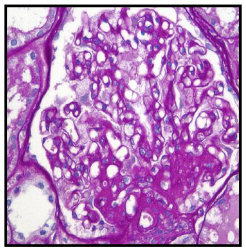
Fabry disease: Renal pathology

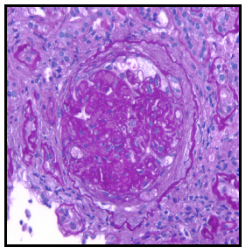
From storage to glomerulosclerosis

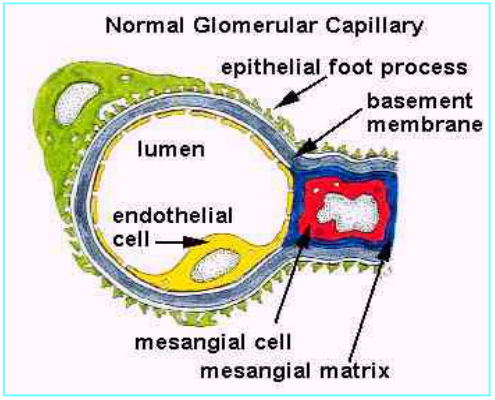








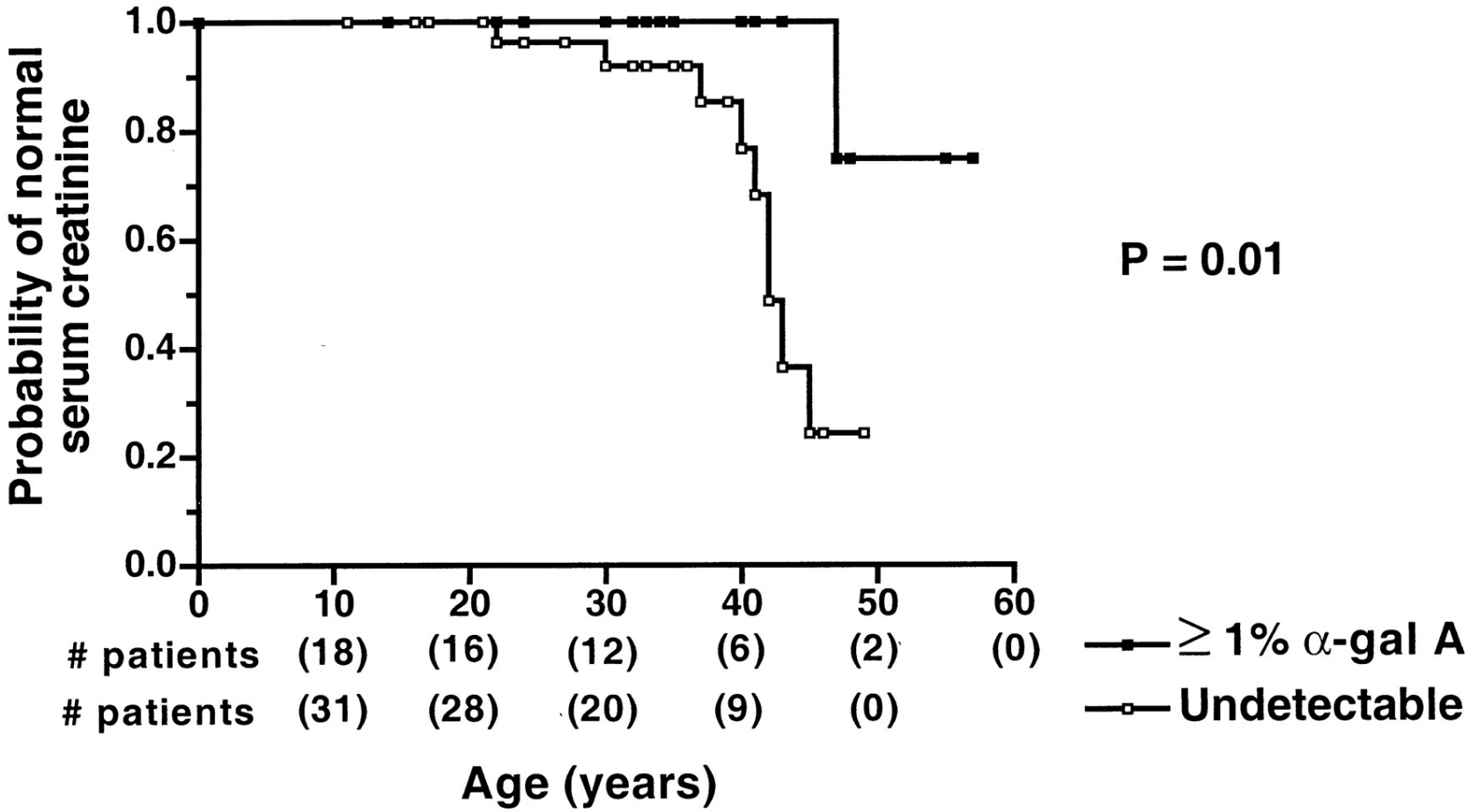




Kaplan-Meier analysis:

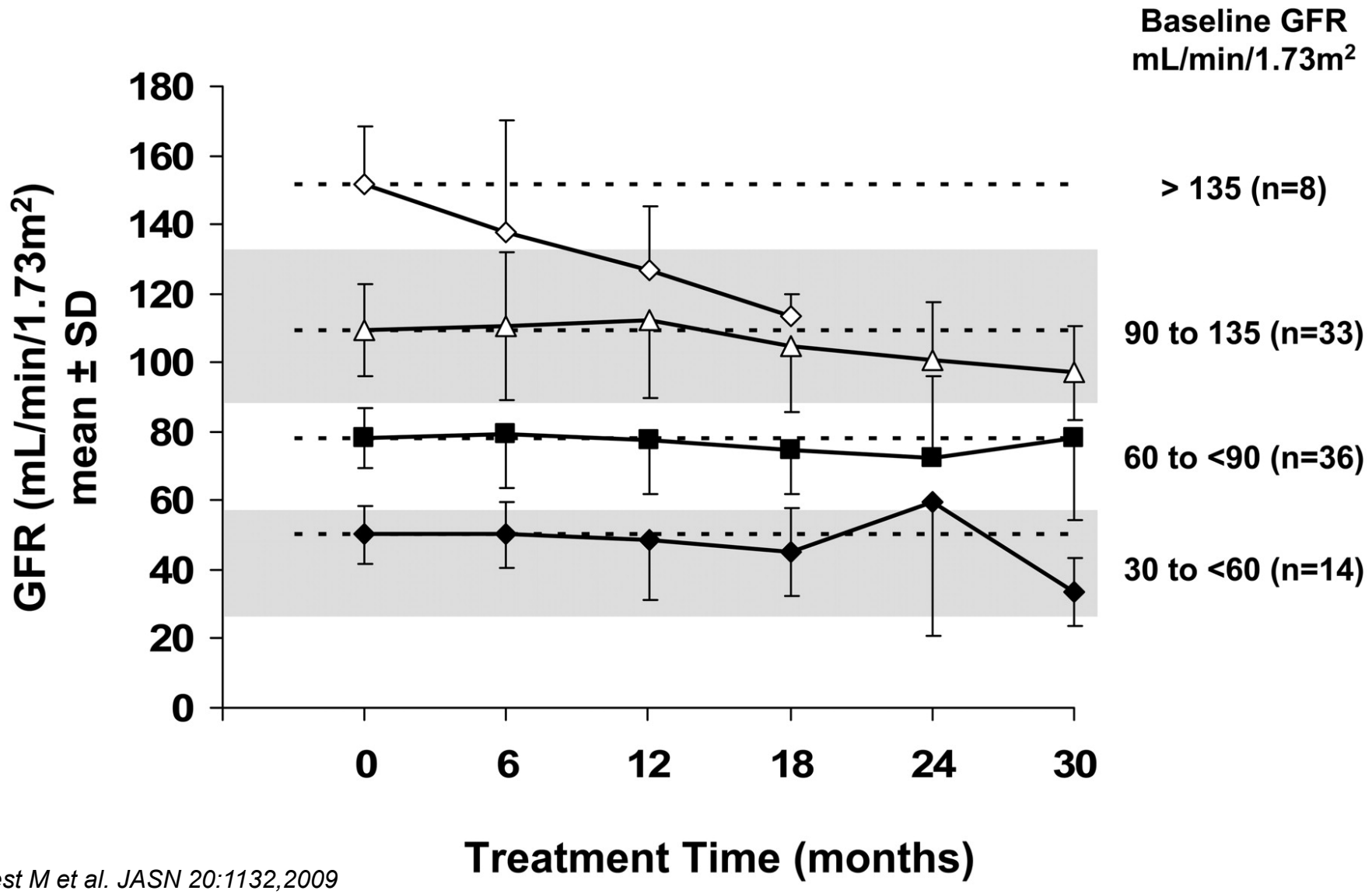
Probability of developing chronic renal insufficiency,

analyzed by residual α-Gal A activity



Branton M et al. JASN 13:S139, 2007

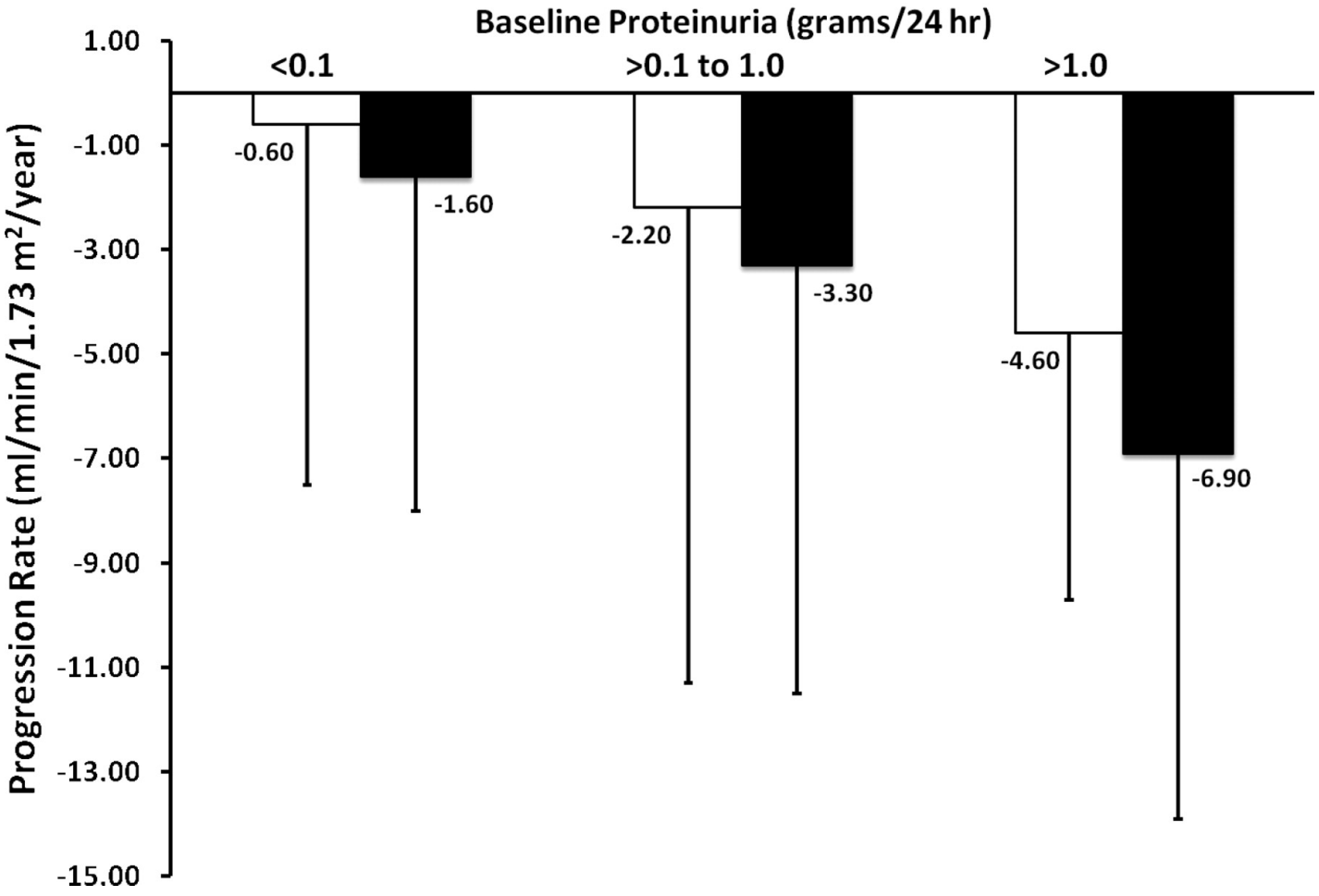
ΔGFR on ERT in male FD patients, stratified according to baseline GFR.



West M et al. JASN 20:1132,2009

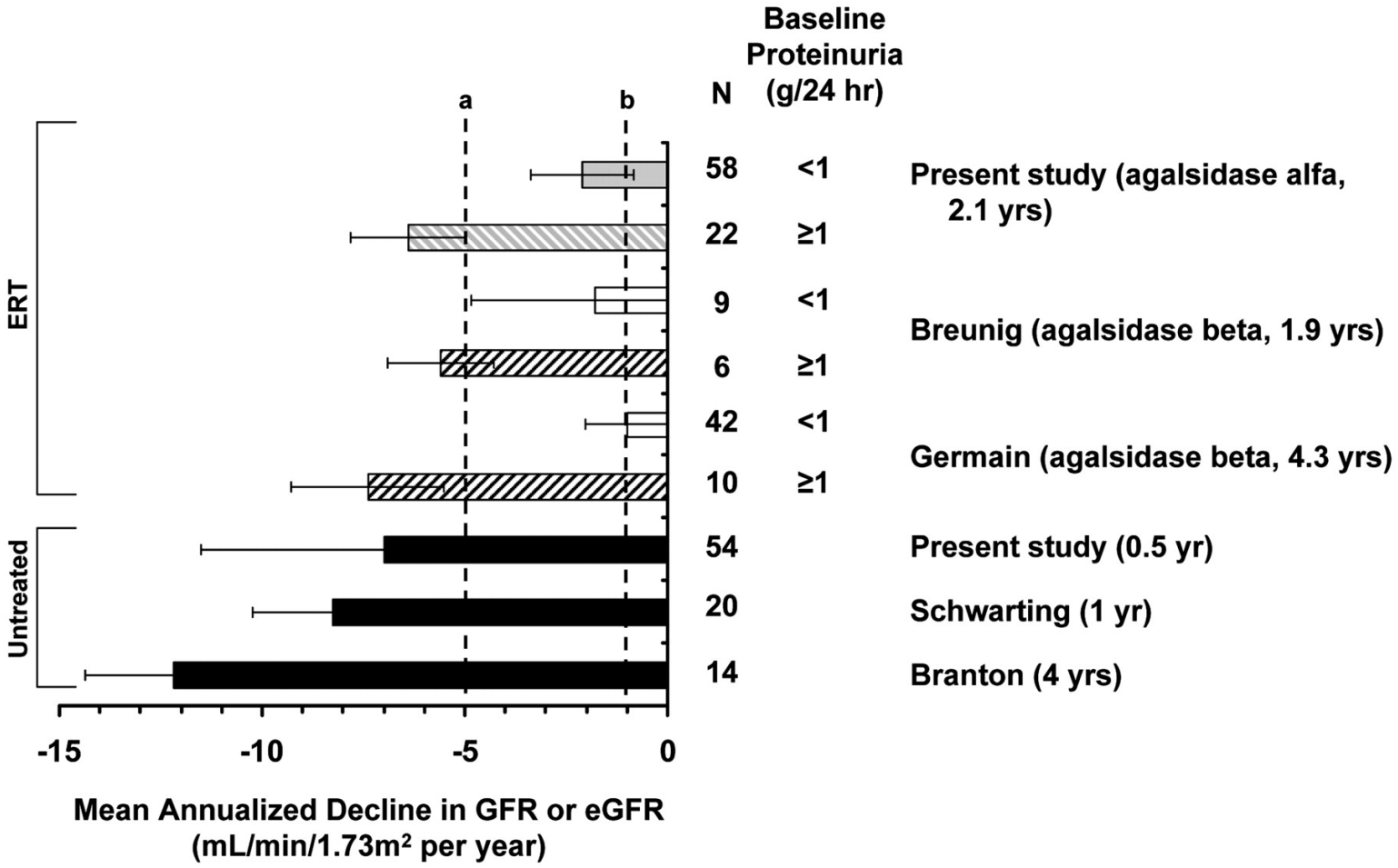
Fabry nephropathy:

Natural history



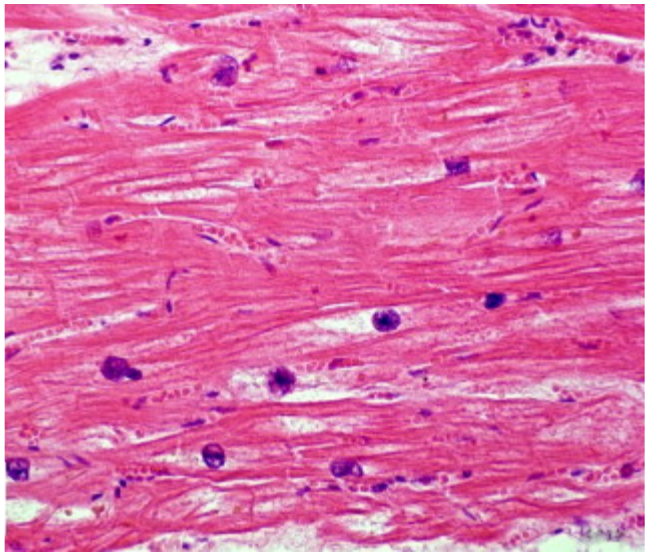
Warnock D G et al. CJASN 5:371,2010

Rates of DGFR in patient with Fabry disease with or without (■) ERT

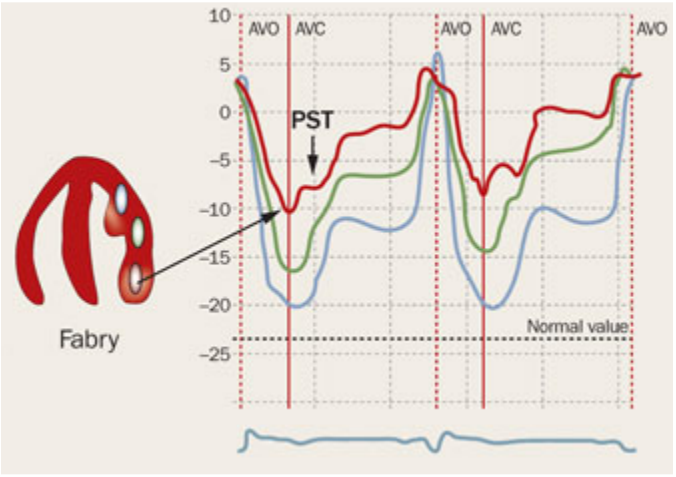


West, M. et al. J Am Soc Nephrol 20:1132-1139,2009

Fabry disease: *Cardiovascular disease*

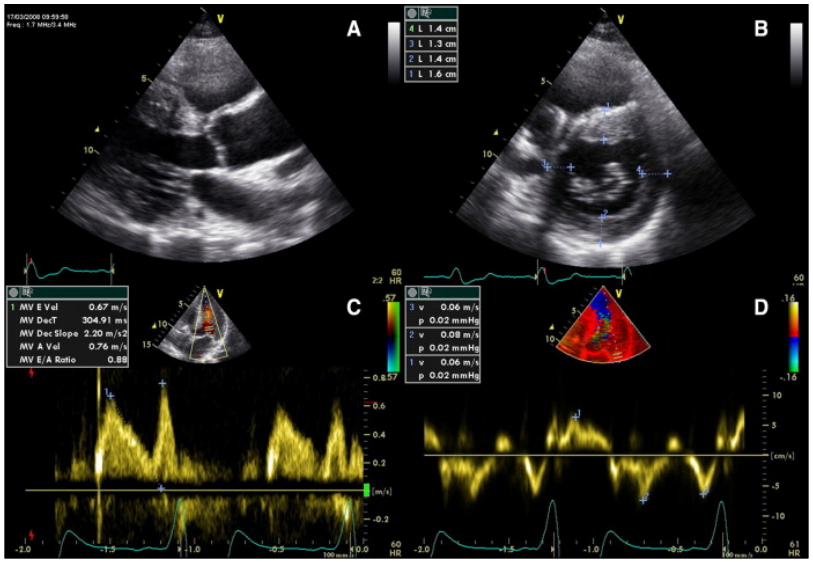


Perinuclear vacuoles (storage) and hypertrophy of cardiomyocytes
Gb3 <2%

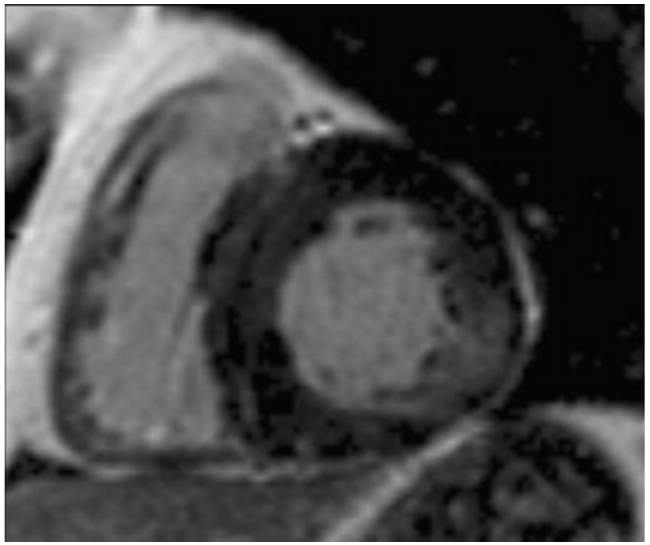


Longitudinal strain curves; showing overall reduced deformation and markedly reduced systolic and postsystolic deformation in the basal (infero)-lateral segment

Fabry disease: *Cardiovascular disease*



Concentric LVH (wall thickness 16 mm). Diastolic dysfunction with an abnormal mitral valve inflow pattern (C); impaired longitudinal systolic function on tissue Doppler imaging (D).

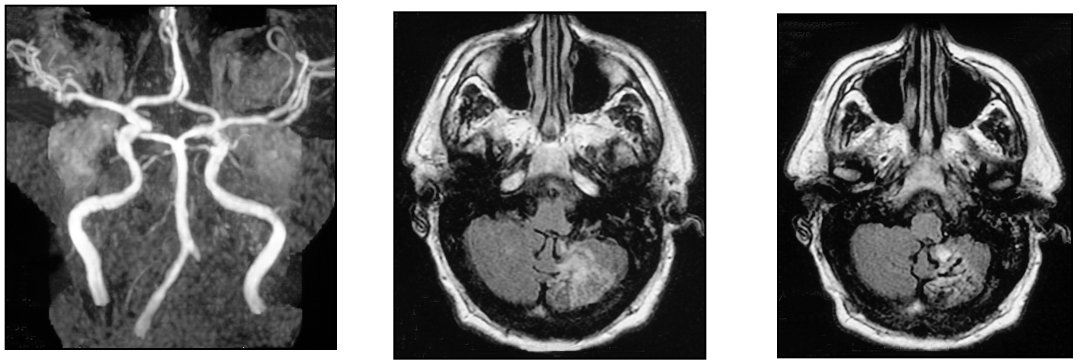


Concentric LVH (wall thickness 20 mm) Late gadolinium enhancement, inferolateral wall from base to midventricle; sparing the endocardium.

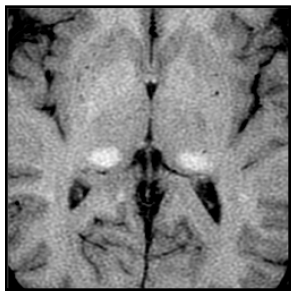
Fabry disease:

Cerebrovascular disease

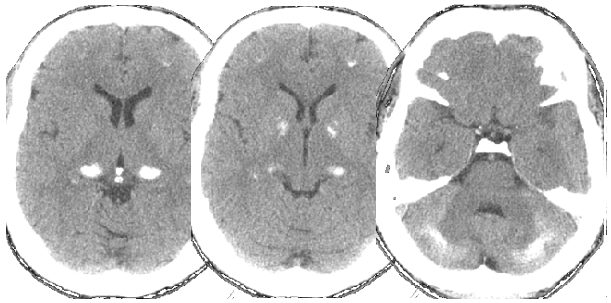
Cerebrovascular Lesions



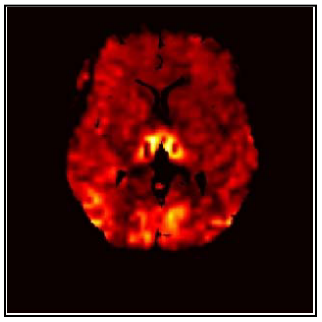
T1-weighted MRI



Head CT

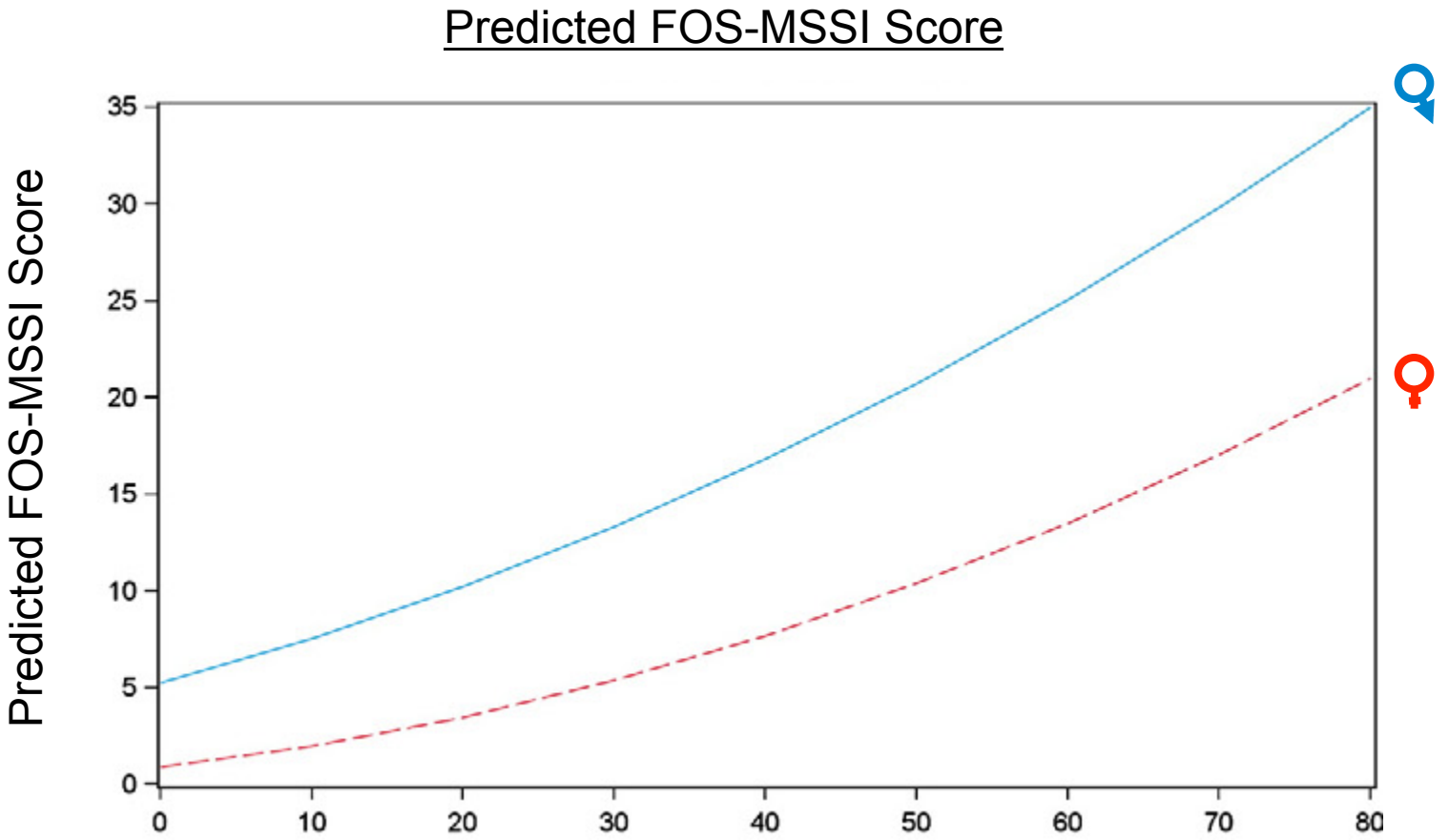


CBF map



Fabry disease :

Age adjusting severity scores



Males = $[2.29 + (0.05*Age)]^2$
Females = $[0.96 + (0.05*Age)]^2$

Hughes DA, et al. Mol Genet Metab. 101(2-3):219,2010

Fabry disease

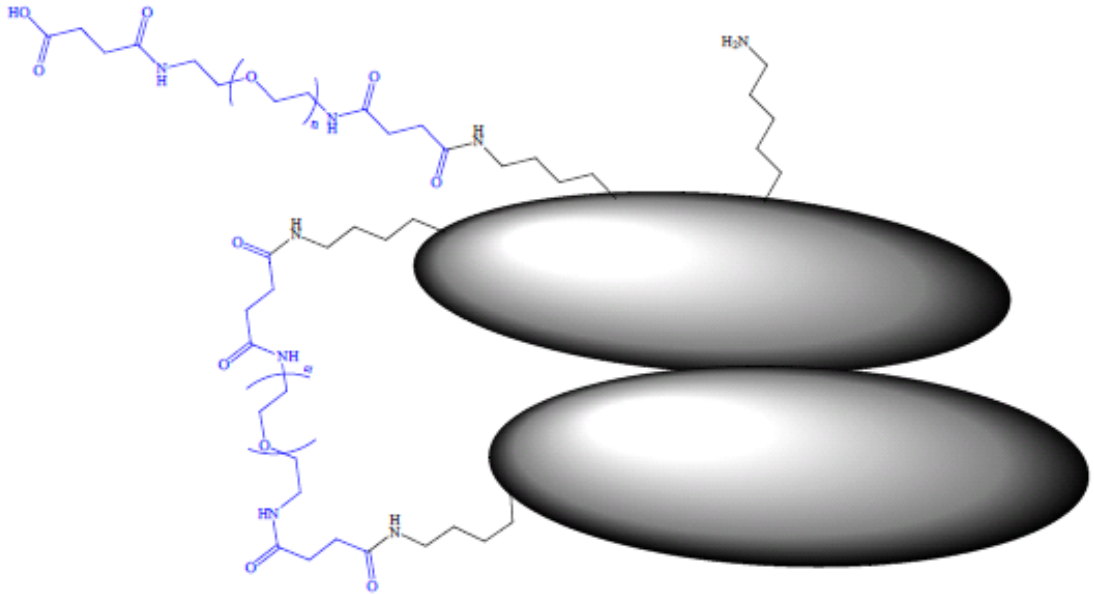
Summary

- Fabry disease is a complex multi-systemic disorder, associated with significant disease burden and shortened lifespan; affecting both males and female, and with symptom onset in childhood
- There are currently two enzyme formulations, which indicate clinical benefit for certain patient groups, using different regimens
- Interestingly, time on therapy appears to have a greater influence on mid term outcome (up to 10 years), rather than enzyme dose; although this needs to be examined in larger cohorts. Moreover, there is a need to stratify patients in according to disease severity at baseline, which appears to be a major determinant of outcome
- Cardiac and cerebrovascular disease continue to be major drivers of morbidity, and renal insufficiency is progressive for those with advanced stages and significant proteinuria
- Antibodies against the infused enzyme, appears to be neutralizing in some cases; based on increased substrate (GL3) excretion,; athough there is no evidence at this time of an adverse influence on outcome

PRX-102 for Fabry Disease

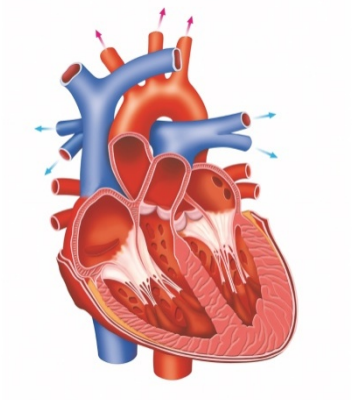
Dr. Einat Almon, Senior Vice President, Product Development, Protalix Biotherapeutics

PRX-102 - A Plant Cell Expressed, Chemically Modified, Human α-Galactosidase for the Treatment of Fabry Disease

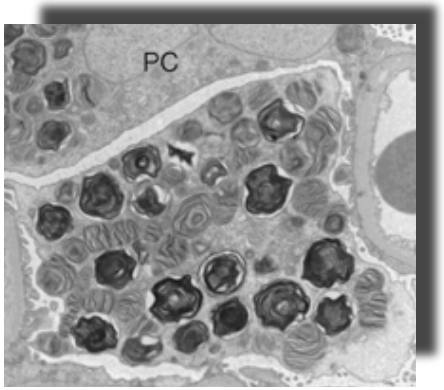


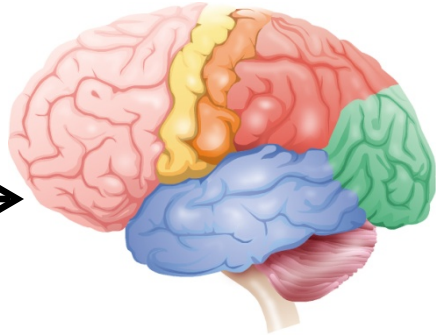
Fabry Disease

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

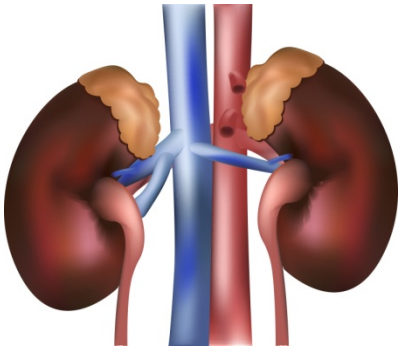


Hypertension and cardiomyopathy





Increased risk of stroke



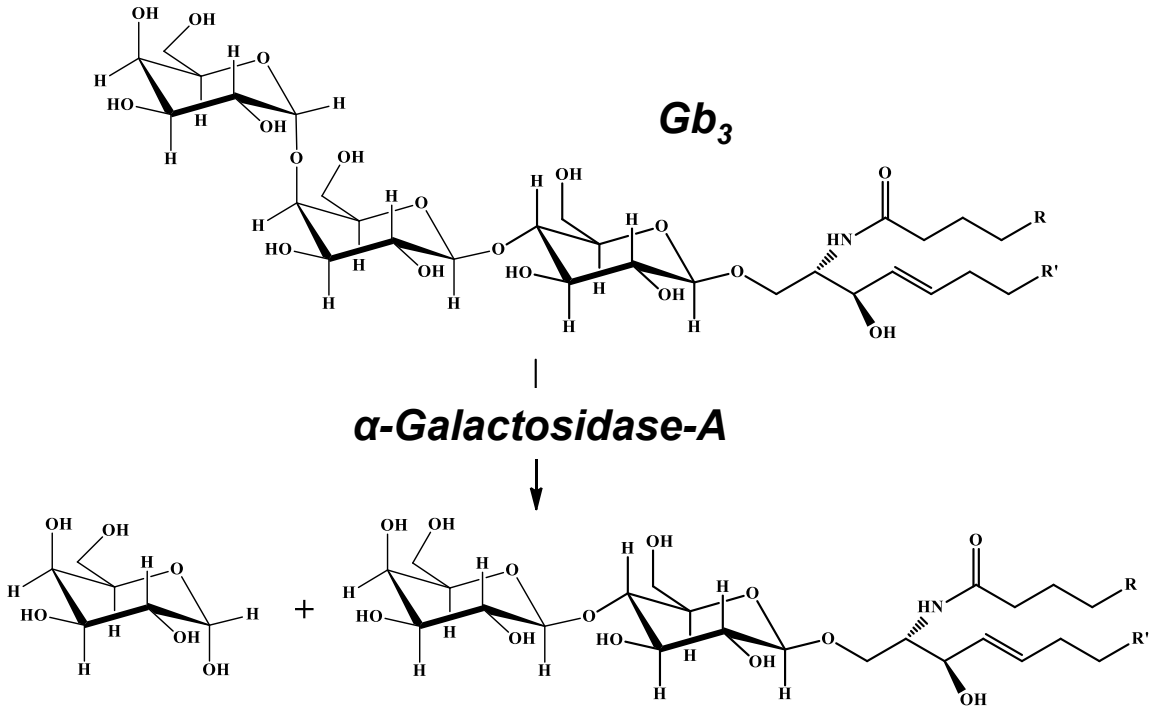
Renal insufficiency and renal failure

Outcome: Poor quality of life - Death

Source: Adopted from Najafian et al., Kidney Int. 2011

α-Galactosidase-A

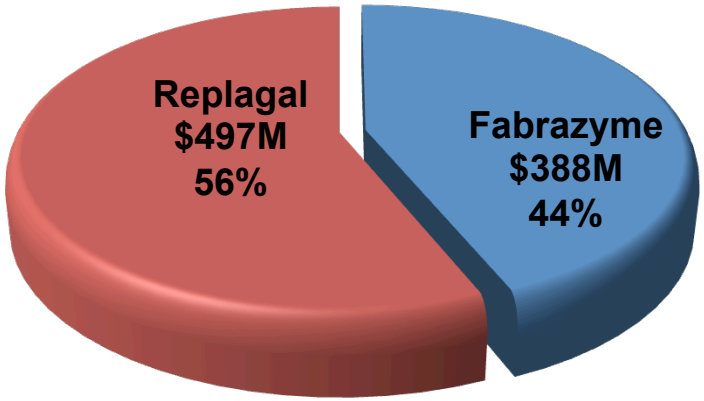
- A non-covalently linked homo-dimer of 398aa each (~96 KDa)
- A lysosomal hydrolase that cleaves a terminal galactose from glycolipids/glycoproteins



Fabry Disease Market

- Annual cost of treatment ~$250,000/patient
- Prevalence – between 1:40,000 – 1:120,000
- Diagnosis rate is rapidly growing (CAGR = 12.8%)
- Market size (2012): ~$900M

2012 Fabry Market share



Product Rationale

Currently available treatment:

- Fabrazyme® (Genzyme)
- Replagal® (Shire) - Not approved in the US
- 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

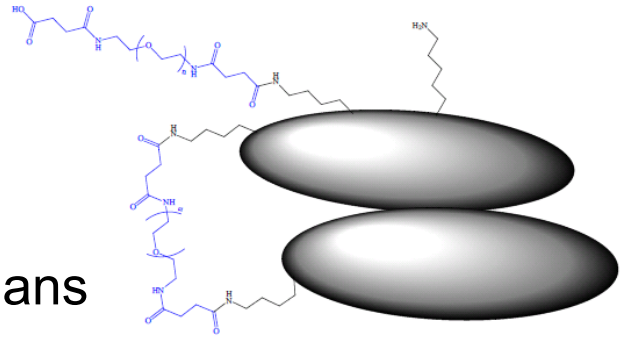
Method:

- Generation of a stable dimer via covalent cross-linking

PRX-102 Product Description

The chemical modification:

- Both protein sub-units are PEGylated , resulting in a covalently bound active and stable dimer



Advantages:

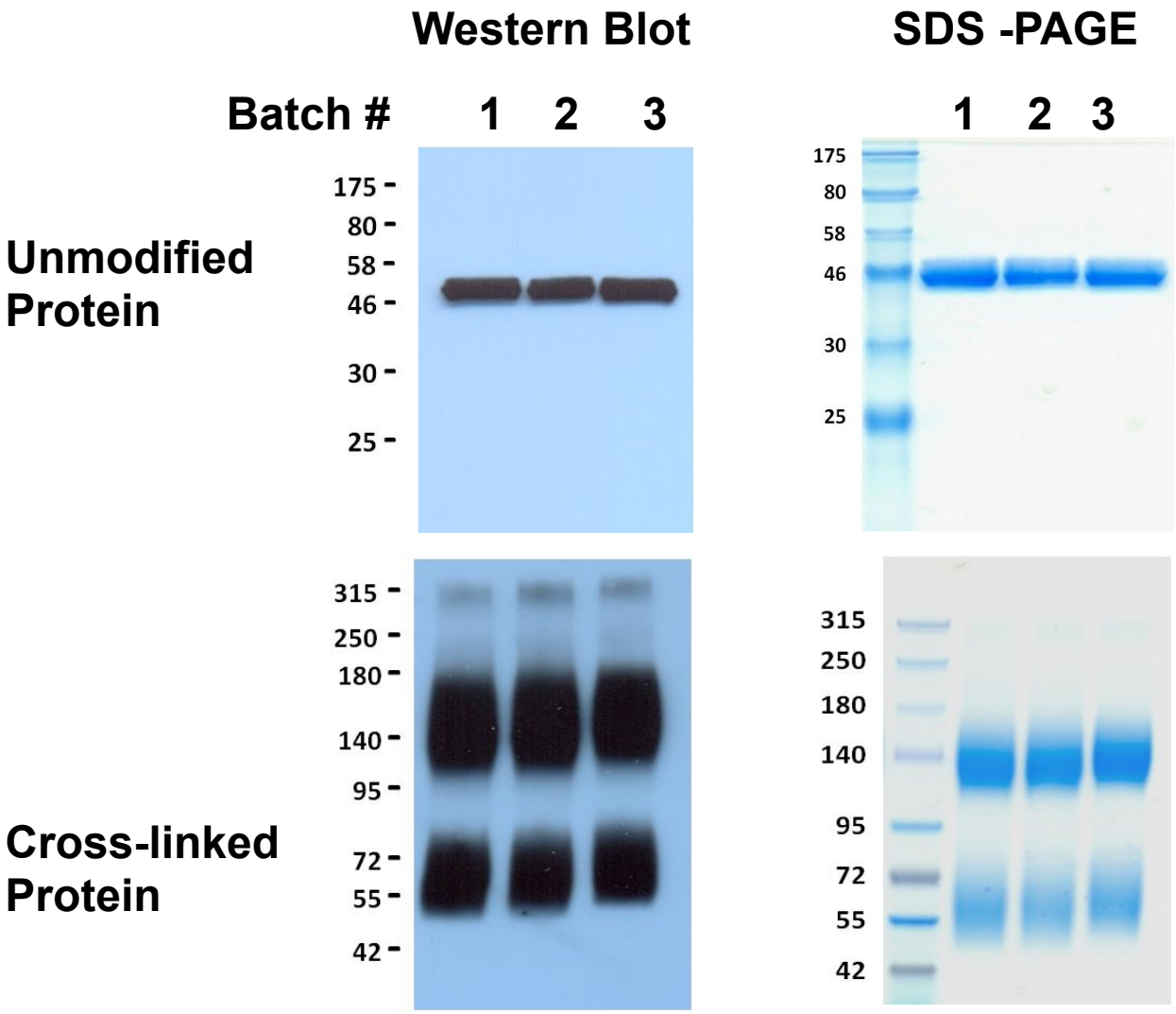
- Improved stability
- Longer circulatory half life
- Enhanced uptake and activity in target organs

PRX-102 properties can potentially lead to:

- Better clinical efficacy
- Different regimen

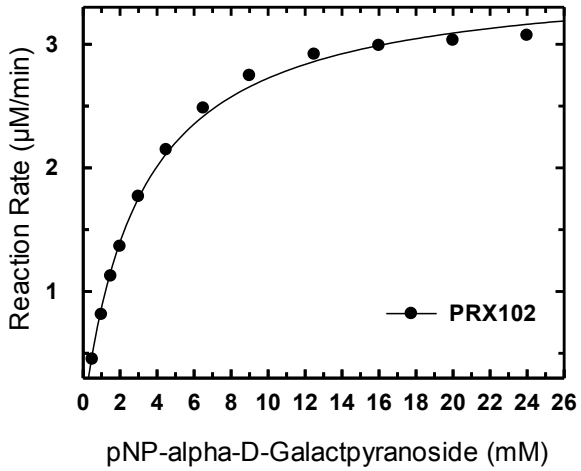
PRODUCT PROFILE

PRX-102 Characterization



PRX-102 Enzyme Kinetics

Michaelis Menten Kinetics



Sample	K_M (µM)	V_{max} (µM/ min)	k_{cat} (sec^{-1})	k_{cat}/K_M (sec^{-1}* mM^{-1})
Replagal®	4443	3.31	52.96	0.011
PRX-102	3285	3.72	59.53	0.018

PRX-102 exhibits similar kinetic properties compared to commercial enzyme

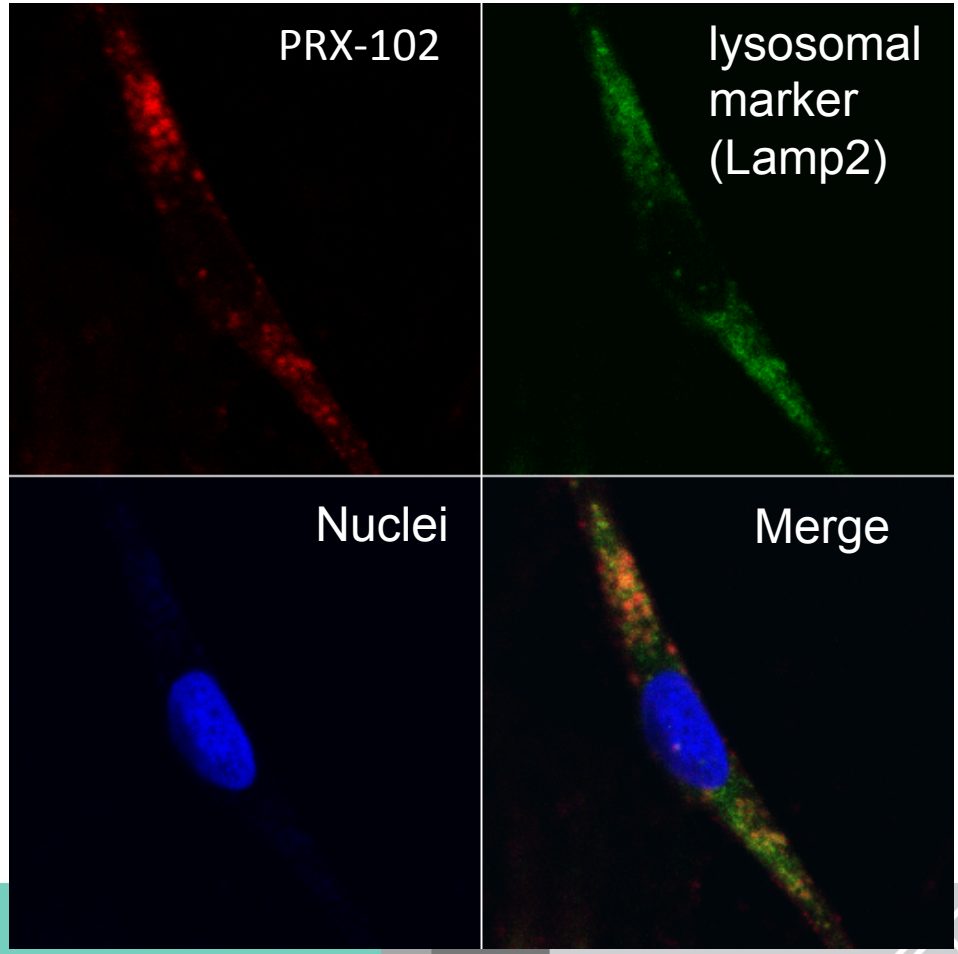
PRX-102 Uptake into Fabry Cells

PRX-102 localization in the lysosome of human Fabry patient fibroblast cells

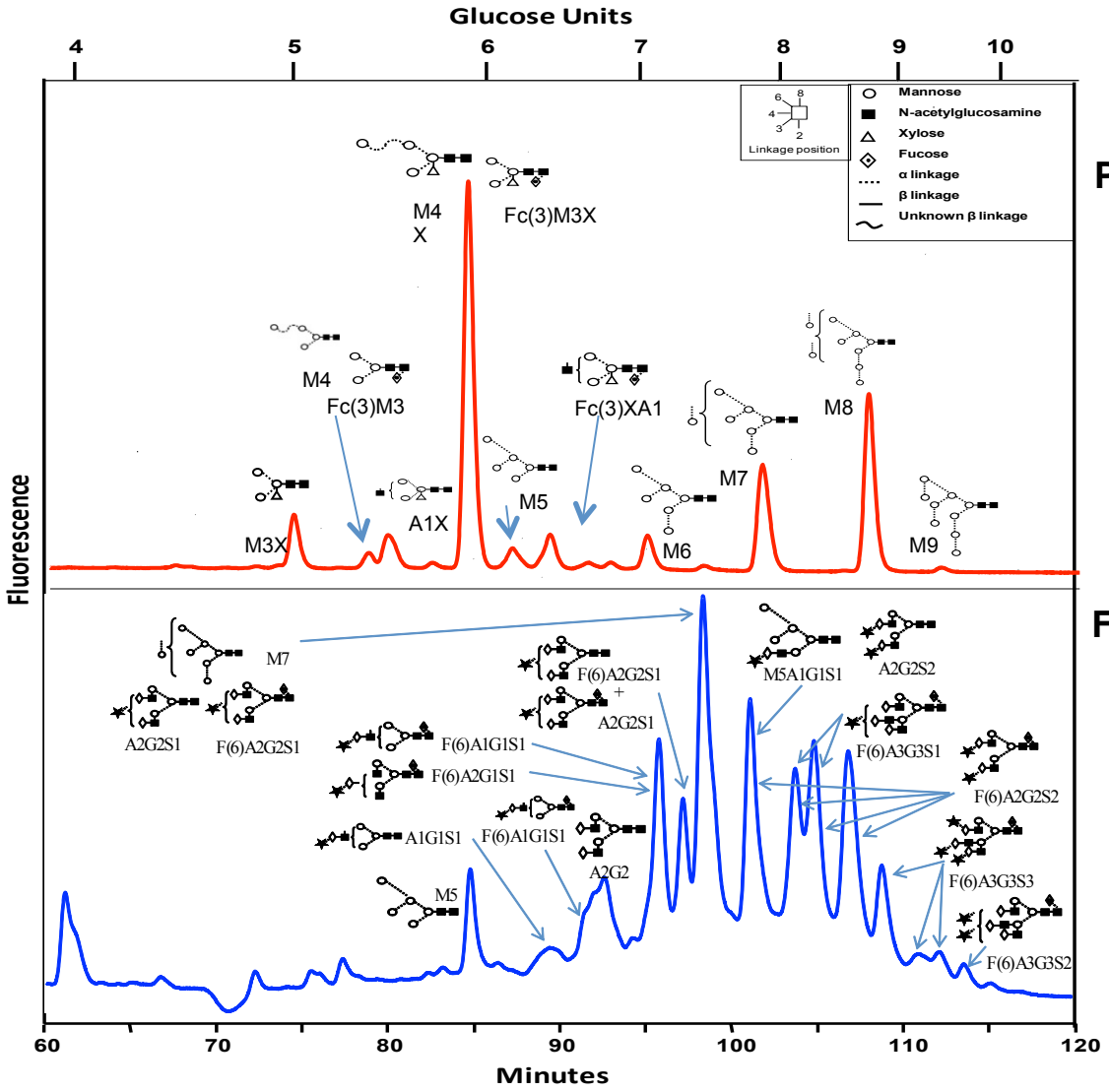
Anti-Gal (red) - PRX-102

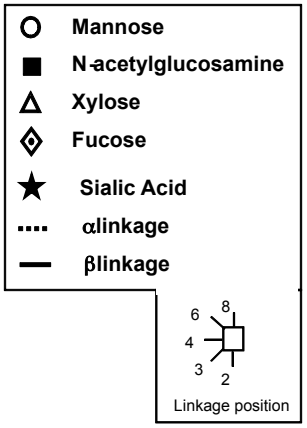
Lamp 2 (green) - Lysosome

Dapi (blue) - Nuclei



Glycosylation Pattern of PRX-102 Vs. Fabrazyme

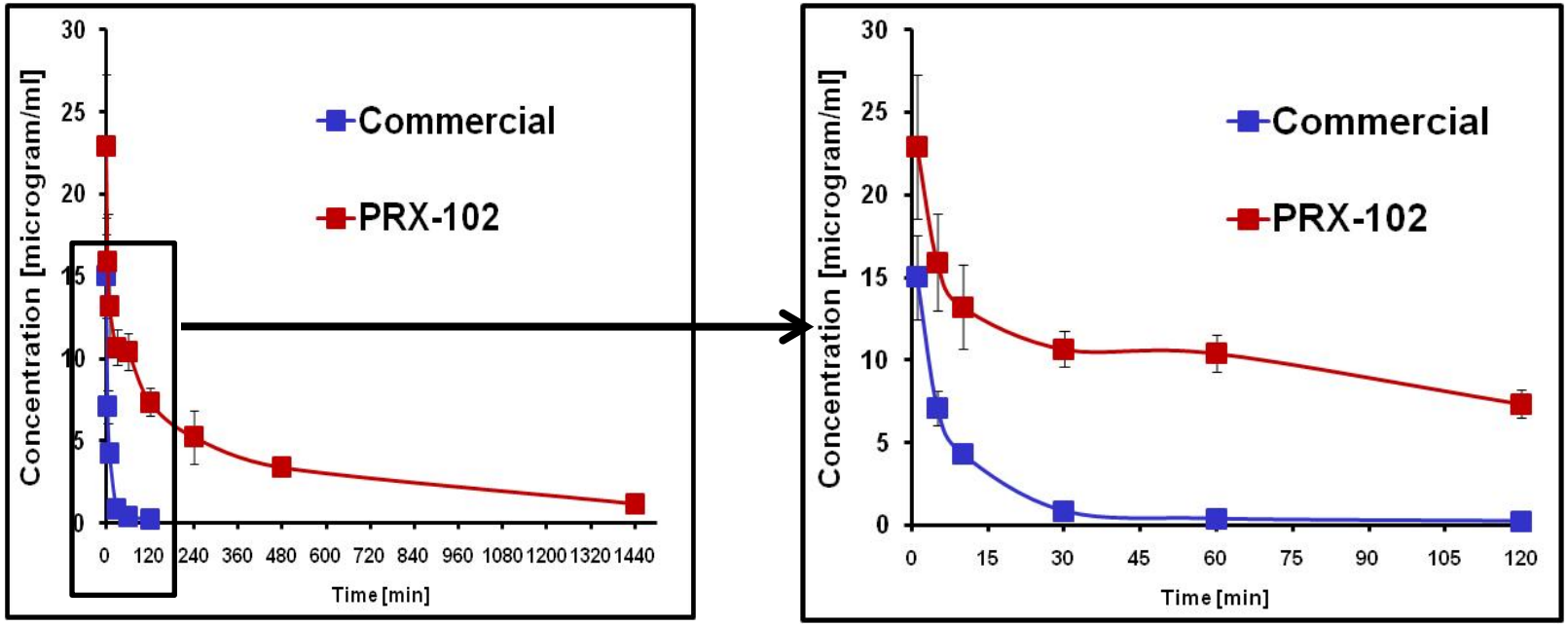




PRE-CLINICAL STUDIES

Improved PK

Prolonged circulatory half-life in Fabry mouse model



Half-life ($t_{1/2}$)

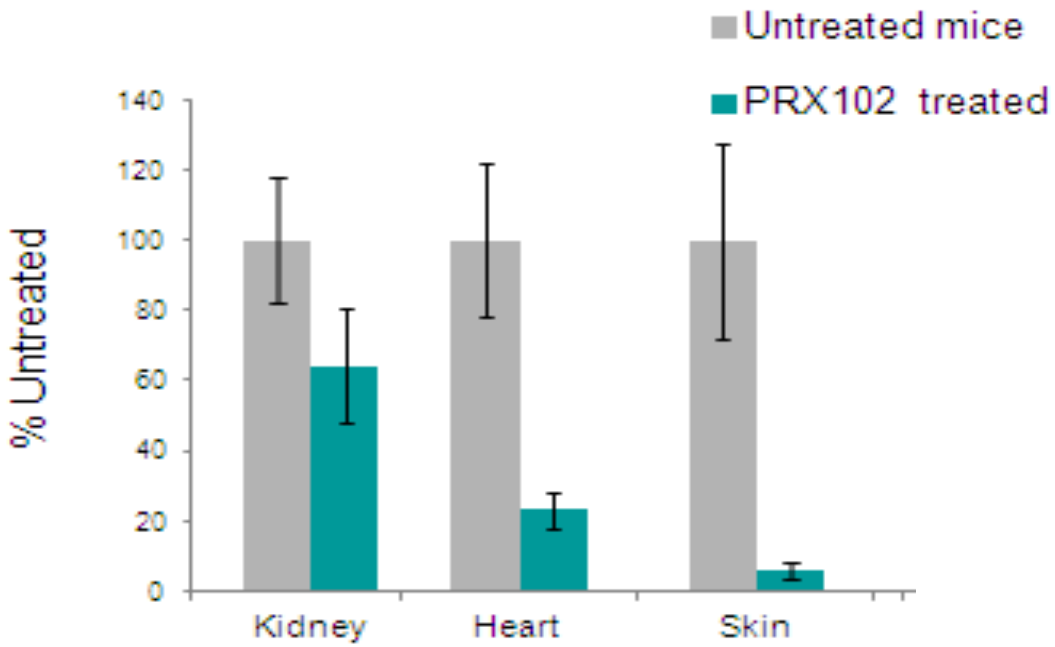
Commercial - 13 min

PRX-102 - 581 min

Bio-Distribution and Efficacy of PRX-102 in Fabry Mice Following Repeat Dosing

Experiment

Four injections, once every two weeks with $2_{mg/kg}$ of either PRX-102 or placebo

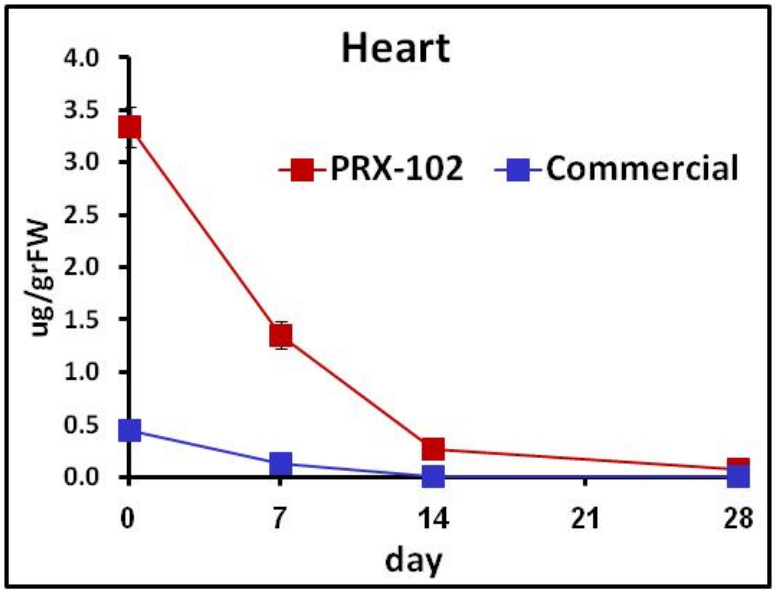


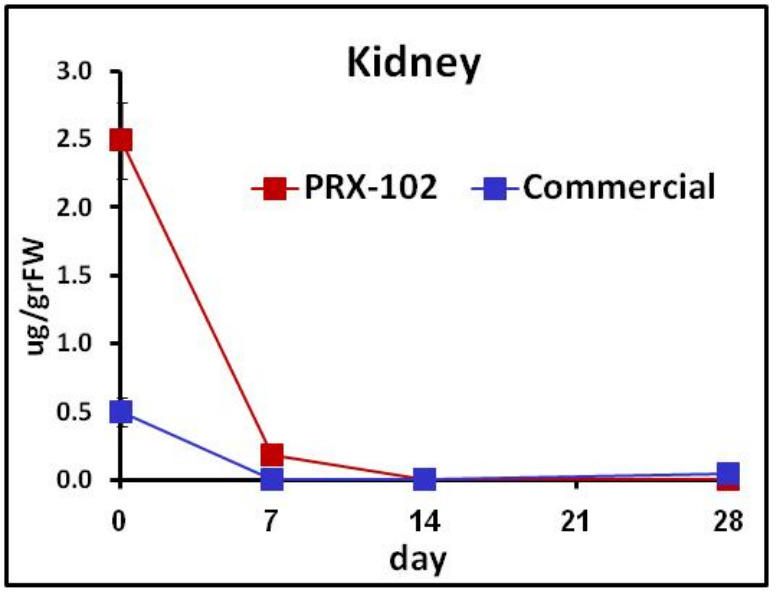
Gb_3 clearance from target tissues following repeated administration of PRX-102

Improved In-vivo Activity
PRX-102 Vs. Replagal

Experiment

Single injection of $2_{mg/kg}$ of either PRX-102 or Replagal





PRX-102 exhibits higher activity levels in target organs over time in Fabry mice

PRX-102 Toxicology Studies

Design:

- Six month studies in two animal species : mice and cynomolgus monkeys
- GLP Tox and TK studies in both species:
  - Three doses (1X (2mg/kg), 5X and 20X of maximal clinical dose)
  - IV every two weeks

Tox results:

- No systemic toxicity was observed in either species
- No safety concerns in monkeys at 20x dose ➔doses up to 2 mg/kg in patients should be well tolerated
- The data support long term clinical trials

CLINICAL DEVELOPMENT

Proposed Clinical Development Plan

Phase 1/2 study

Open Label, Dose Ranging

- Patients who complete the study will be offered the opportunity to enroll in an extension study

Phase 3 Pivotal Study

Double Blind, Active Controlled

- Patients who complete the study will be offered the opportunity to enroll in an extension study

PRX-102 Clinical Plan Outline

Phase 1/2:

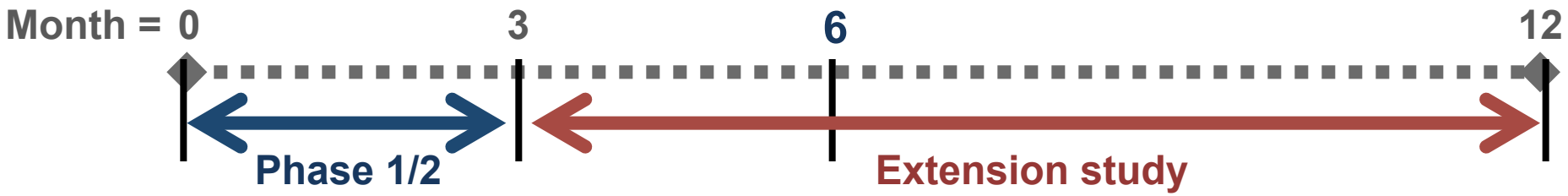
- 18 adult men and women patients (6/group),
- IV infusion once every two weeks
- Three doses (0.2$_{mg/Kg}$,1$_{mg/Kg}$, 2$_{mg/Kg}$)
- Duration - 12 weeks (7 infusions, 3 months)

Extension study:

- 18 patients, IV infusion once every two weeks, at same doses as in Phase 1/2
- Duration - 38 weeks (20 infusions, 9 months)

Study evaluation

- Gb3 in urine and blood, lyso-Gb3 in blood, pain, cardiac MRI
- Skin and kidney biopsies (after 6 months)



PRX-102 Clinical Development Status

- Ongoing phase I/II trial in Fabry patients (under IND)
- Current recruiting sites:
  - Three sites in the United States
  - One site in South America
  - One site in the United Kingdom
  - One site in Australia
- Additional sites pending

Oral GCD for Gaucher Disease

Dr. Yoseph Shaaltiel, Executive Vice President, Research and Development, Protalix Biotherapeutics

PRX-112 - Oral Delivery of Plant Glucocerebrosidase (prGCD) for the Treatment of Gaucher Disease

Oral Delivery of Therapeutic Proteins

The plant cell advantage:

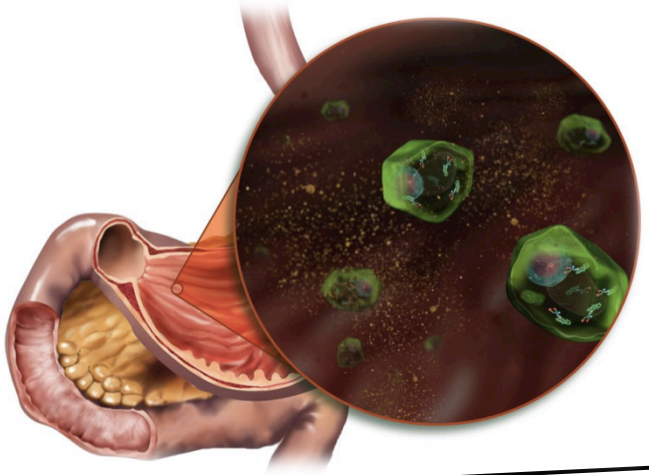
- The concept: Plant cell wall (cellulose) serves as protective agent against the gastric environment
- Can serve as a natural vehicle for oral administration

Three requirements for oral delivery of protein therapeutics:

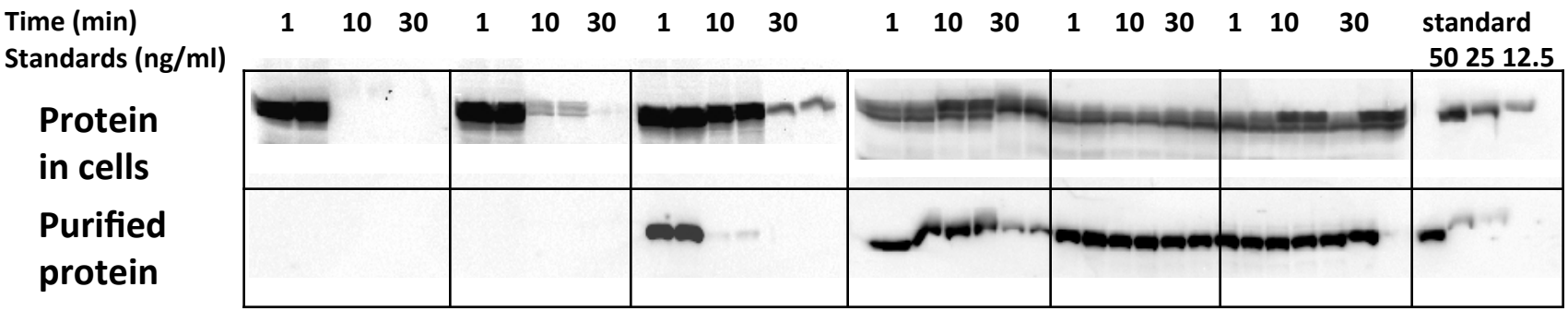
- Protein must survive the gastric environment
- Protein must be released into the intestine from the cells
- Protein must be able to cross the intestinal wall and remain active

Ability to Survive the Gastric Environment

Various proteins naturally encapsulated in plant cells were incubated in a "*simulated gastric fluid*" to asses the protective nature of the plant cell wall

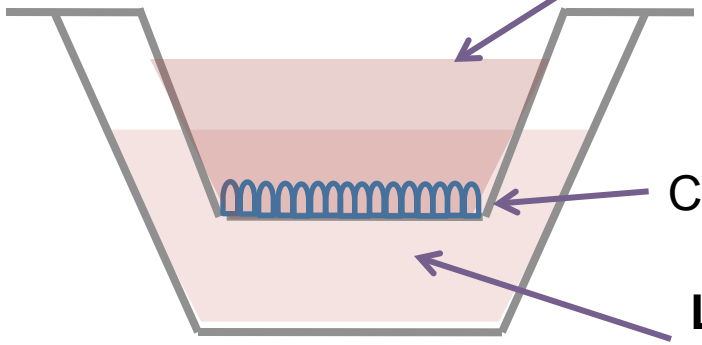


pH gradient Low → High



Cellular Assay That Mimics Crossing the Epithelial Barrier

Protein is added to upper chamber



Upper chamber medium:
Simulated intestinal fluid

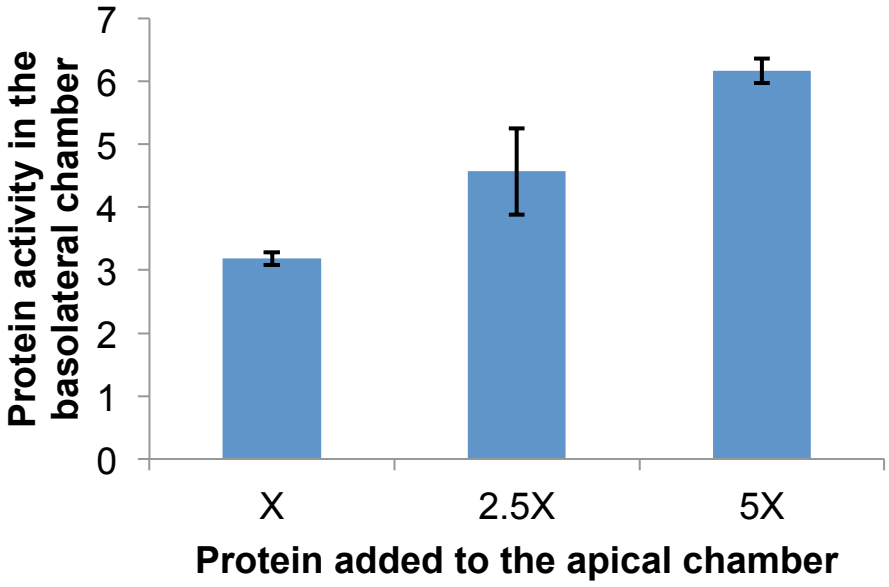
CaCo-2 epithelial cells on membrane

Lower chamber medium:
HBSS pH 7.4 + 4% BSA

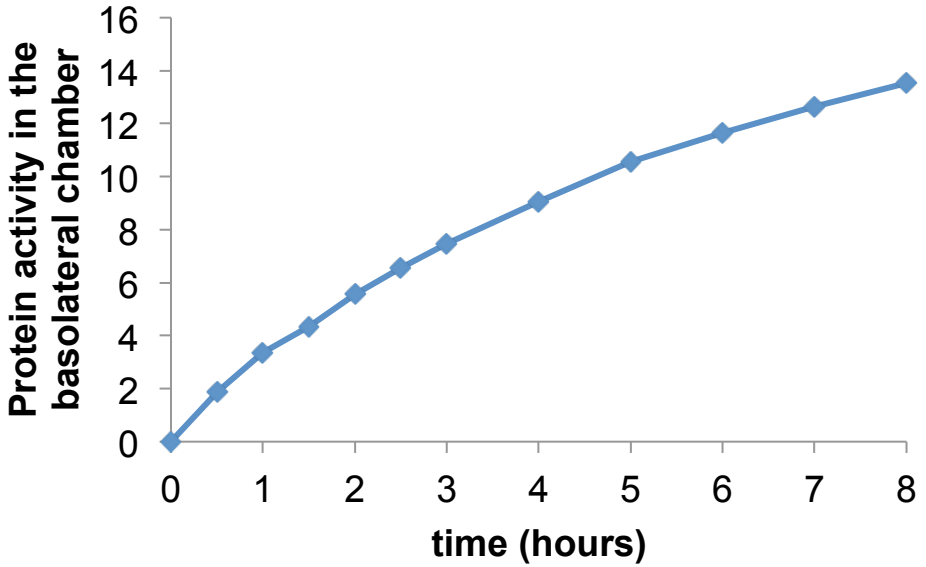
Protein absorption is tested

Crossing the Epithelial Barrier (Caco-2 cell model)

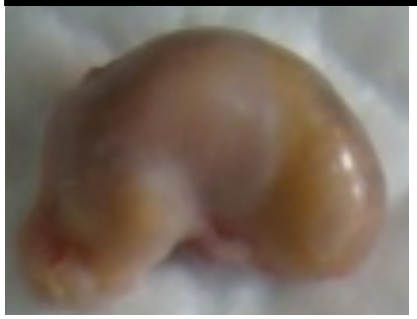
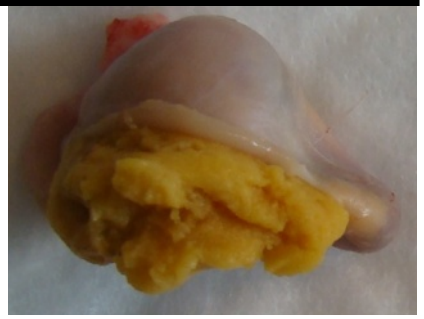
1. Dose response:
Protein added to chamber at different concentrations. Transcytosis is measured after 2 hours at 37°C

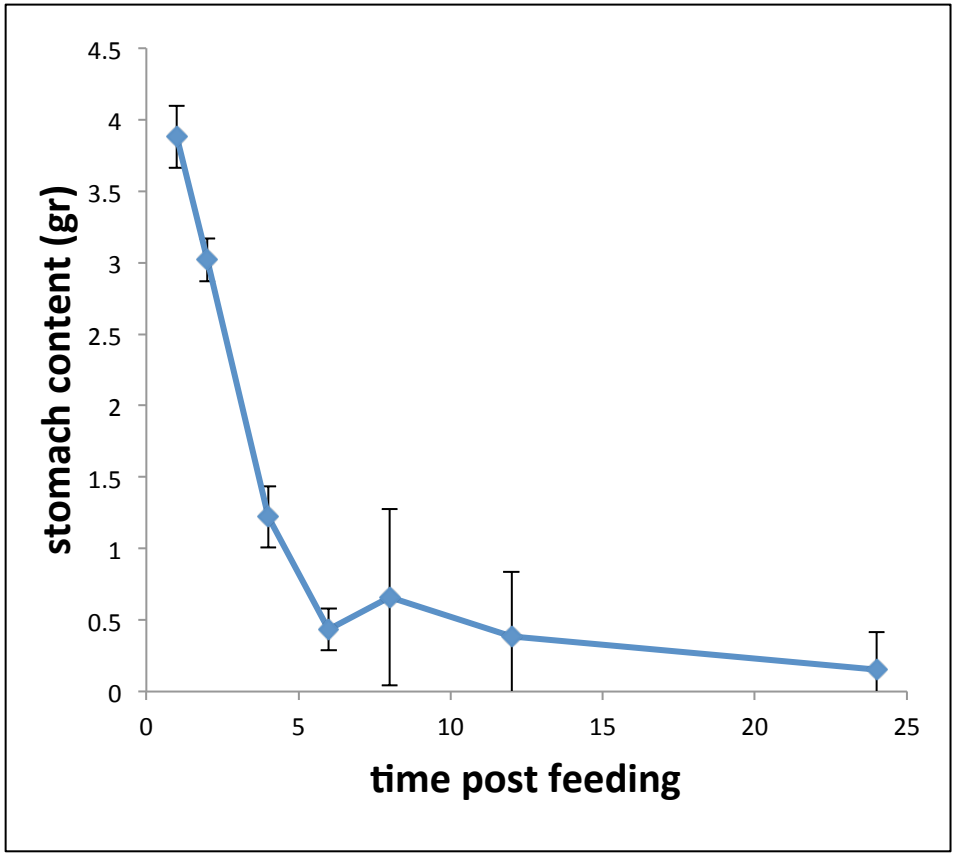


2. Time lapse:
Protein added to chamber.
Transcytosis is measured after the indicated times at 37°C

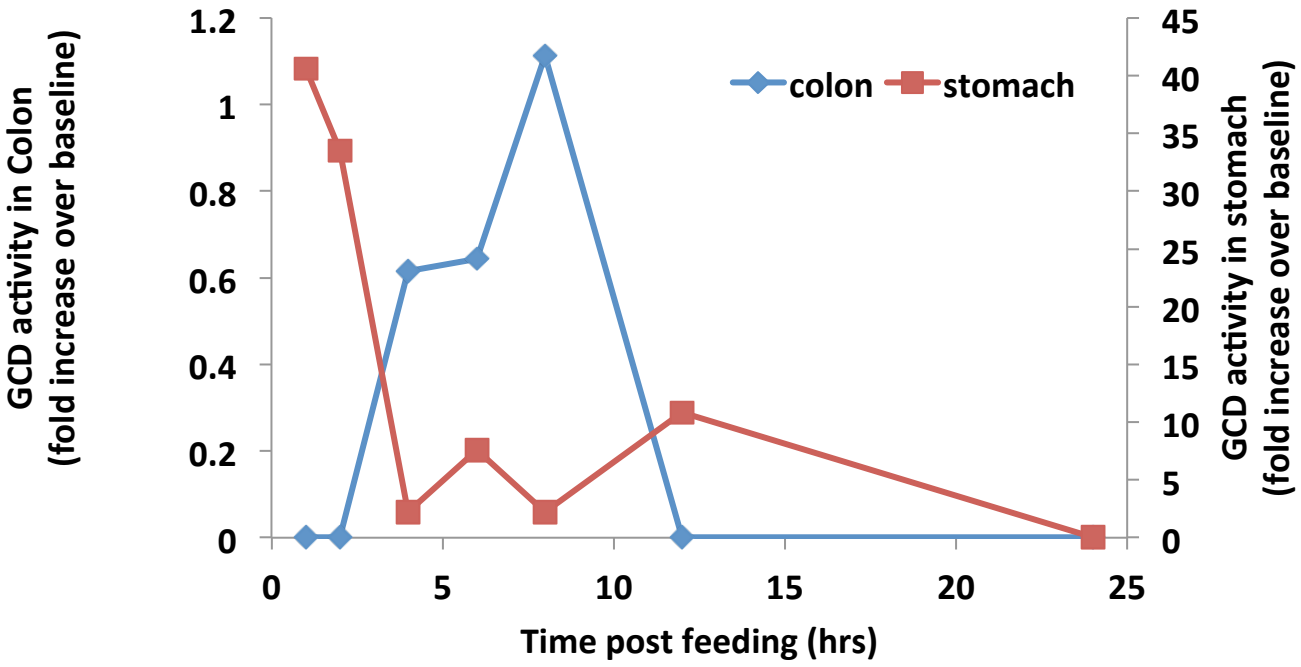


Timeline of Food Passing the Stomach

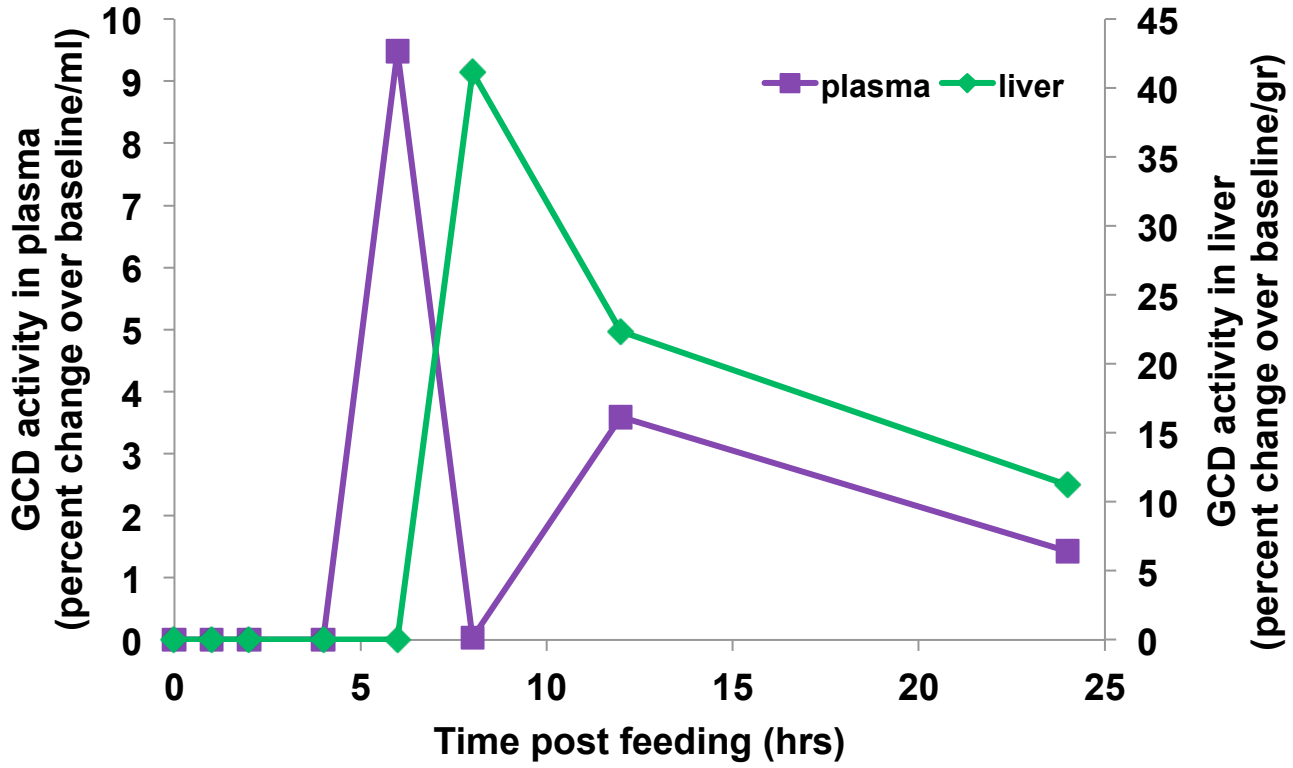
Stomach	Open stomach
	



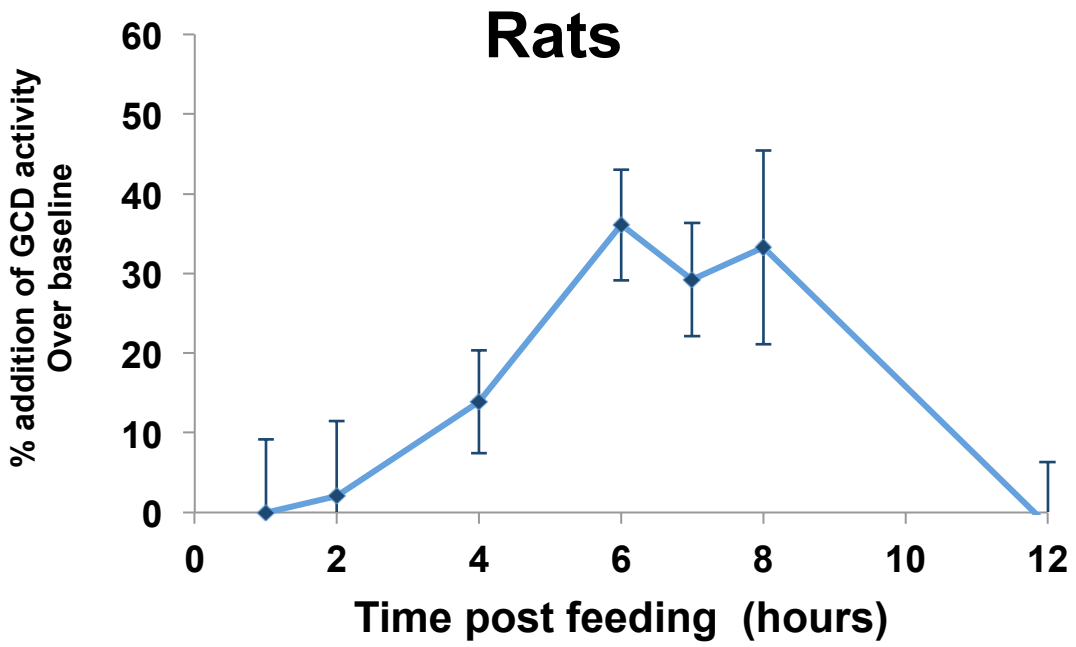
prGCD Activity in the GI Tract



prGCD Activity in Plasma and Target Organs

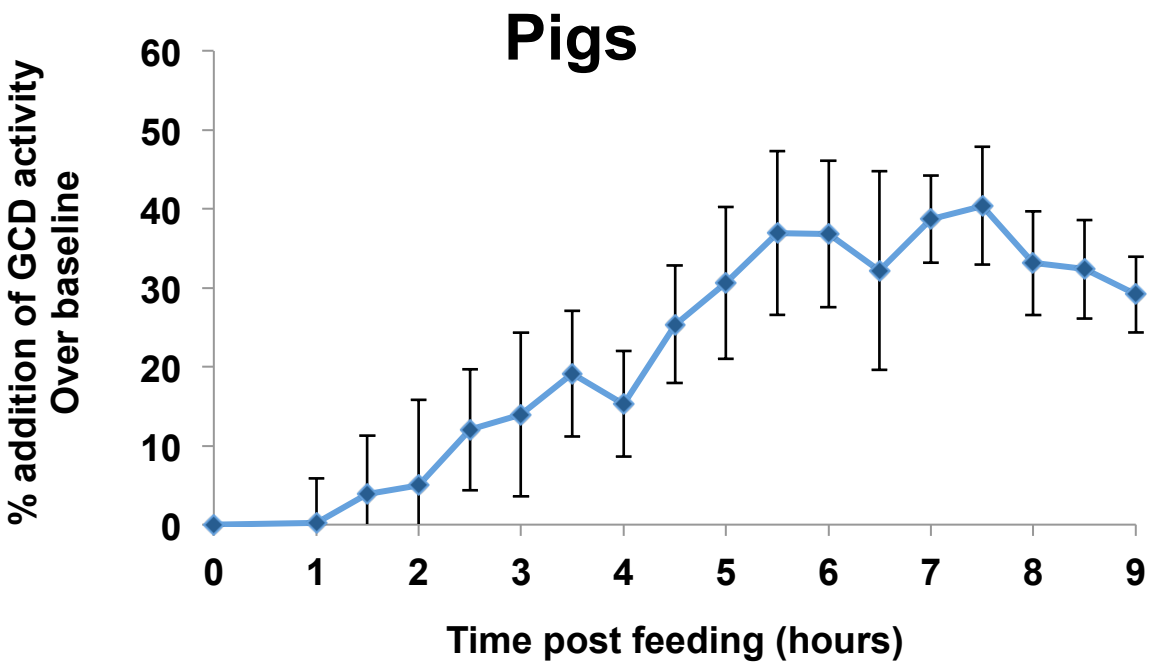


PK Experiments in Rodents



- Rats were fed lyophilized plant cells expressing prGCD
- Animals were assayed for the presence of prGCD in their plasma

PK experiments in Large Animals

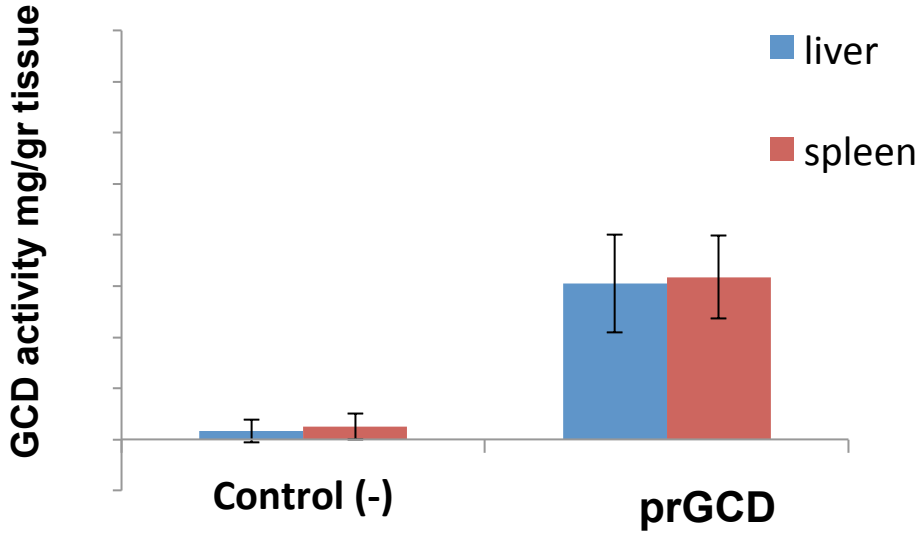


- Animals were fed lyophilized plant cells expressing prGCD
- Animals were assayed for the presence of prGCD in the plasma for several hours post feeding

prGCD Feeding Experiment in Rats

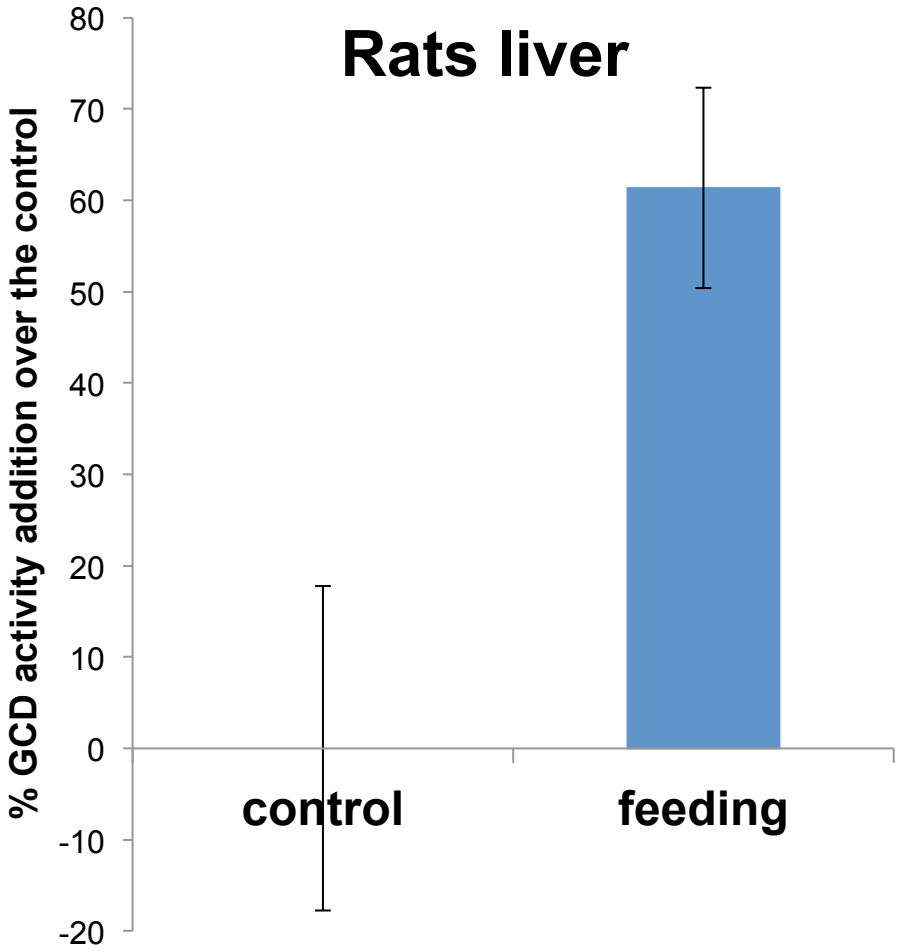
Experiment plan:

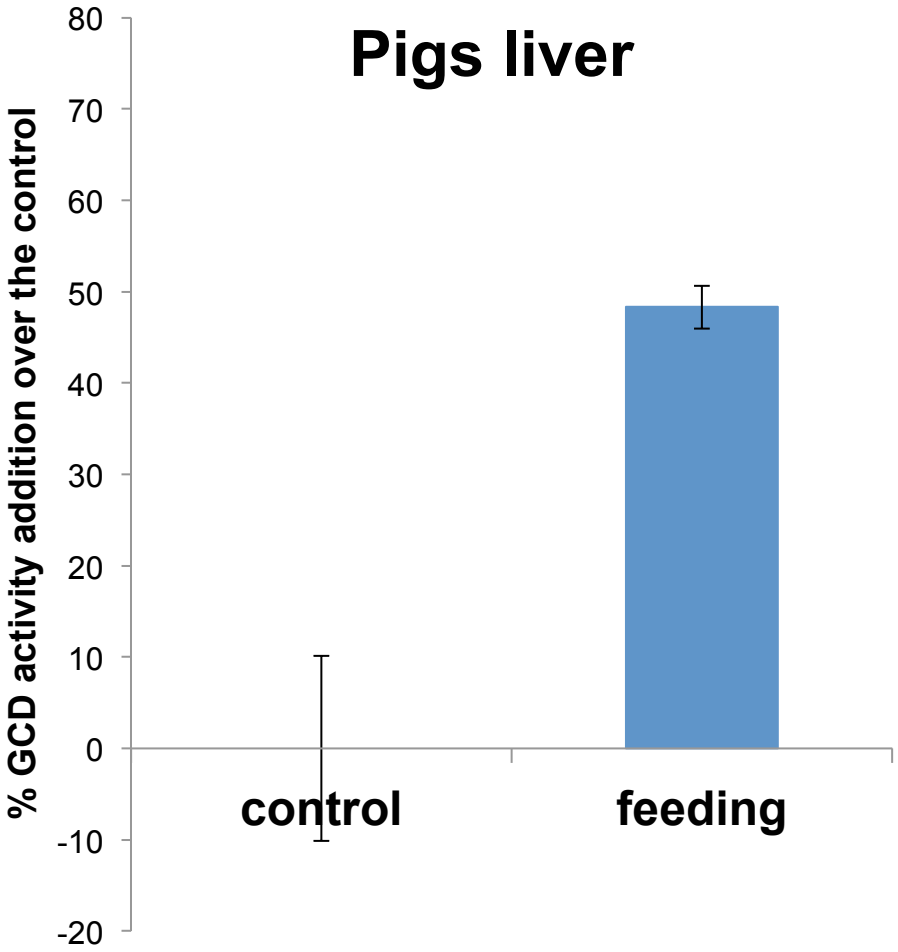
- Rats were fed with lyophilized carrot cells +/- prGCD;
- Amounts of cell consumption were recorded
- Feeding duration: twice with a six-hour interval
- 2 hours following 2nd feeding, prGCD activity was measured in extracted organs



Active prGCD is found in target organs after feeding

prGCD Activity in Target Organs





Summary

Animal studies of Oral prGCD demonstrate the following:

- Absorbance of GCD in the plasma (PK)
- Active prGCD detected in Gaucher target organs *in-vivo*

Oral Delivery of prGCD for the treatment of Gaucher Disease

Prof. Ari Zimran
Director, Gaucher Clinic
Shaare Zedek Medical Center
Jerusalem, Israel

Disclosure

Receives consultancy fees and has options in Protalix Biotherapeutics and member of the Scientific Advisory Board; receives support from Genzyme/Sanofi for participation in the ICGG registry & from SHGT for GOS; honoraria; Pfizer and SHGT.

Oral delivery of therapeutics proteins

- Long time goal for the biopharmaceutical industry
- Currently very limited success
- Answers a desire of patients for oral treatment
- A safe, non invasive method of delivery of protein drugs
- Allows daily intake and slow, continuous drug delivery
- High patient compliance

Oral ERT for Gaucher disease

ERT - gold standard for treatment of Gaucher disease

3 approved ERTs

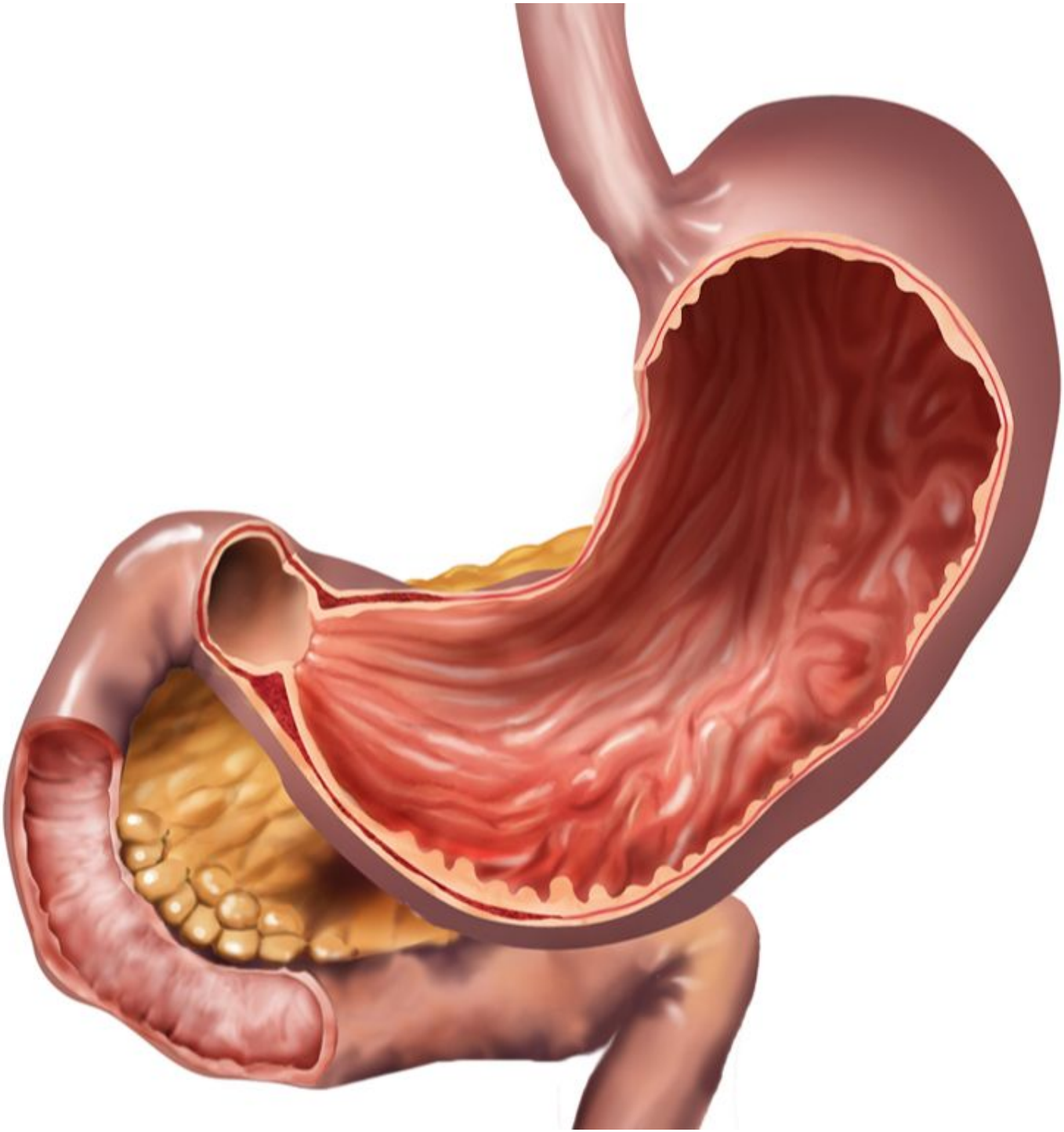
- all safe and efficient
- all administered by IV infusion every 2 weeks

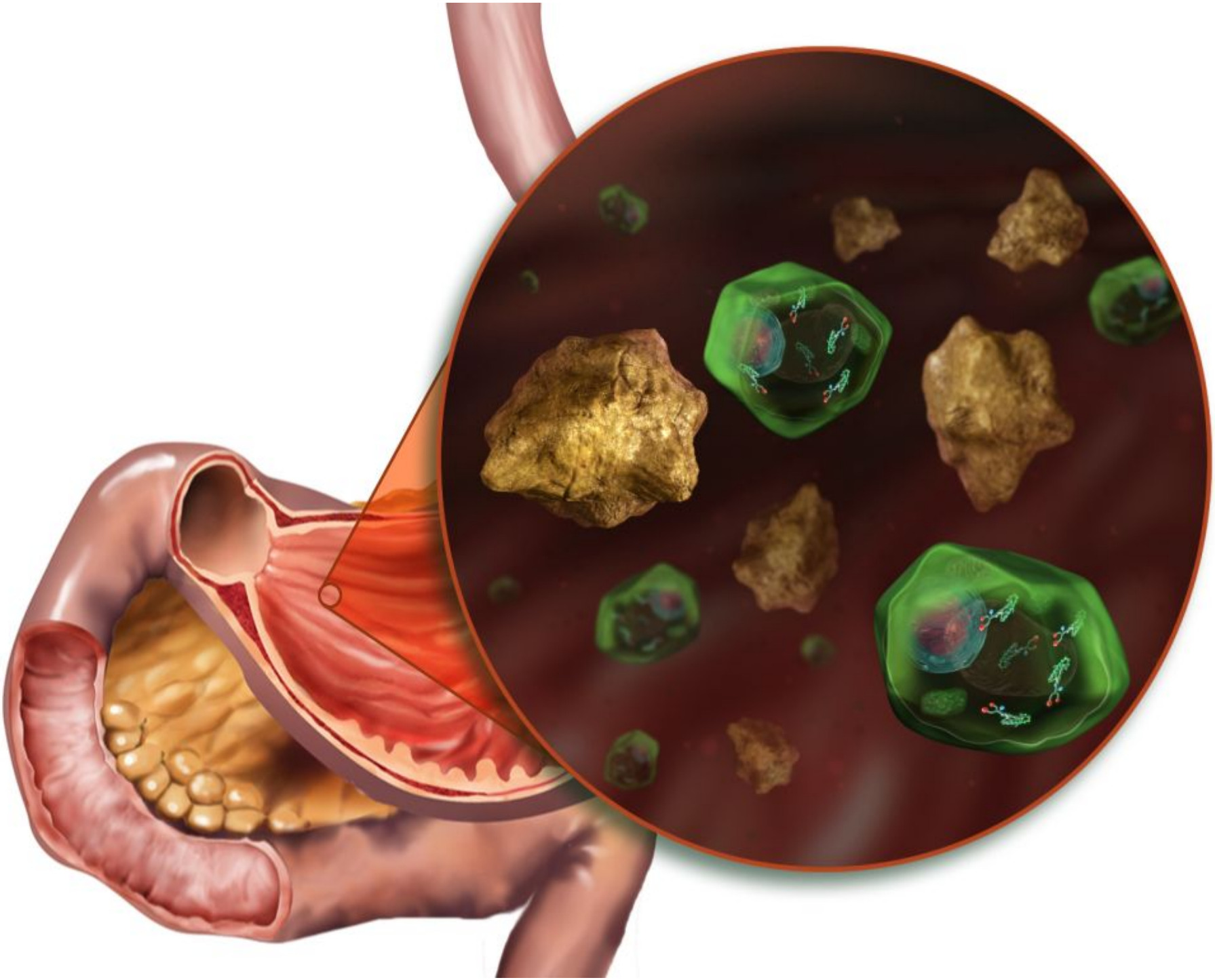
Advantages of orally administered ERT

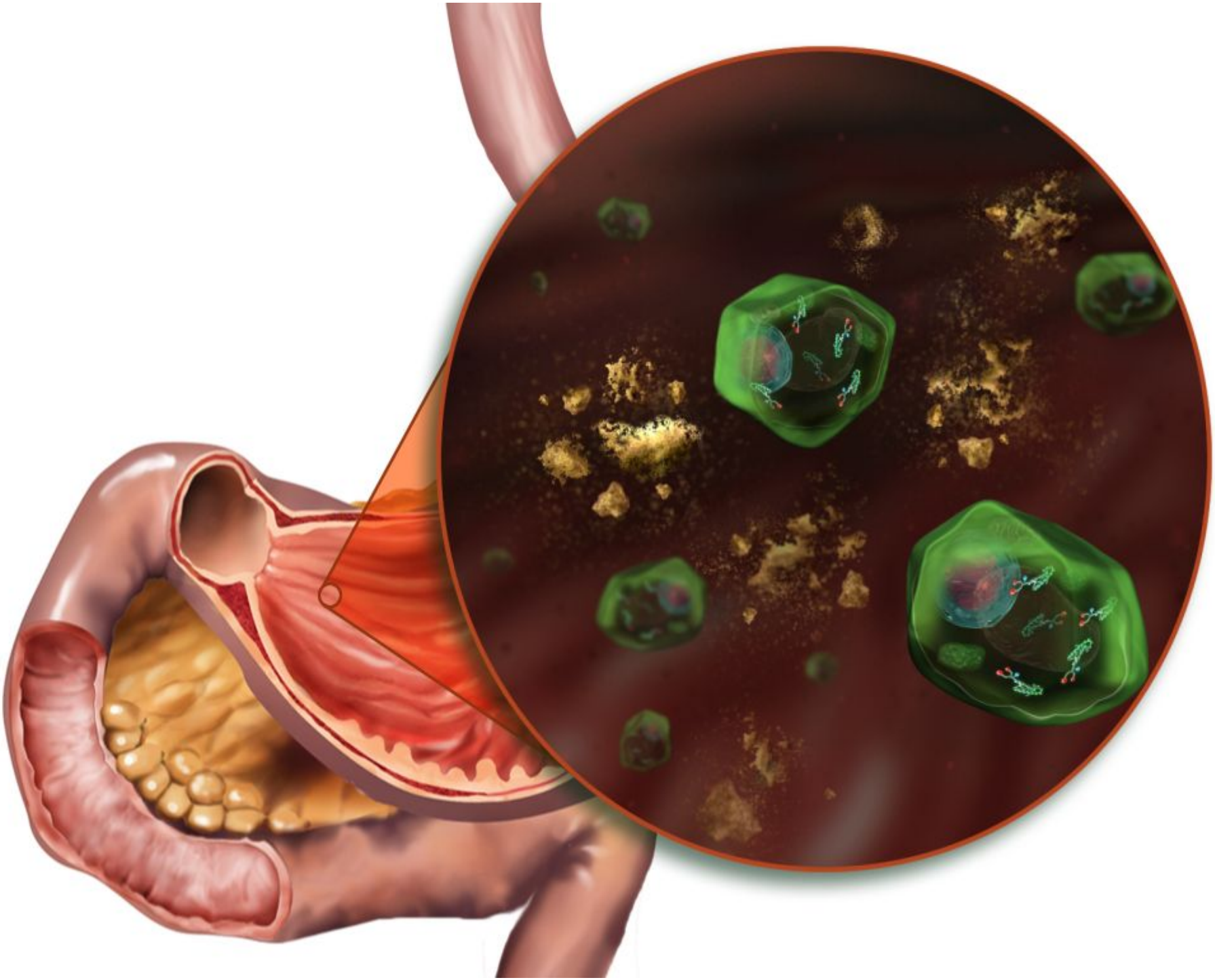
- well-established therapy mechanism
- no limitations of the intravenous administration
- continuous enzyme secretion to blood

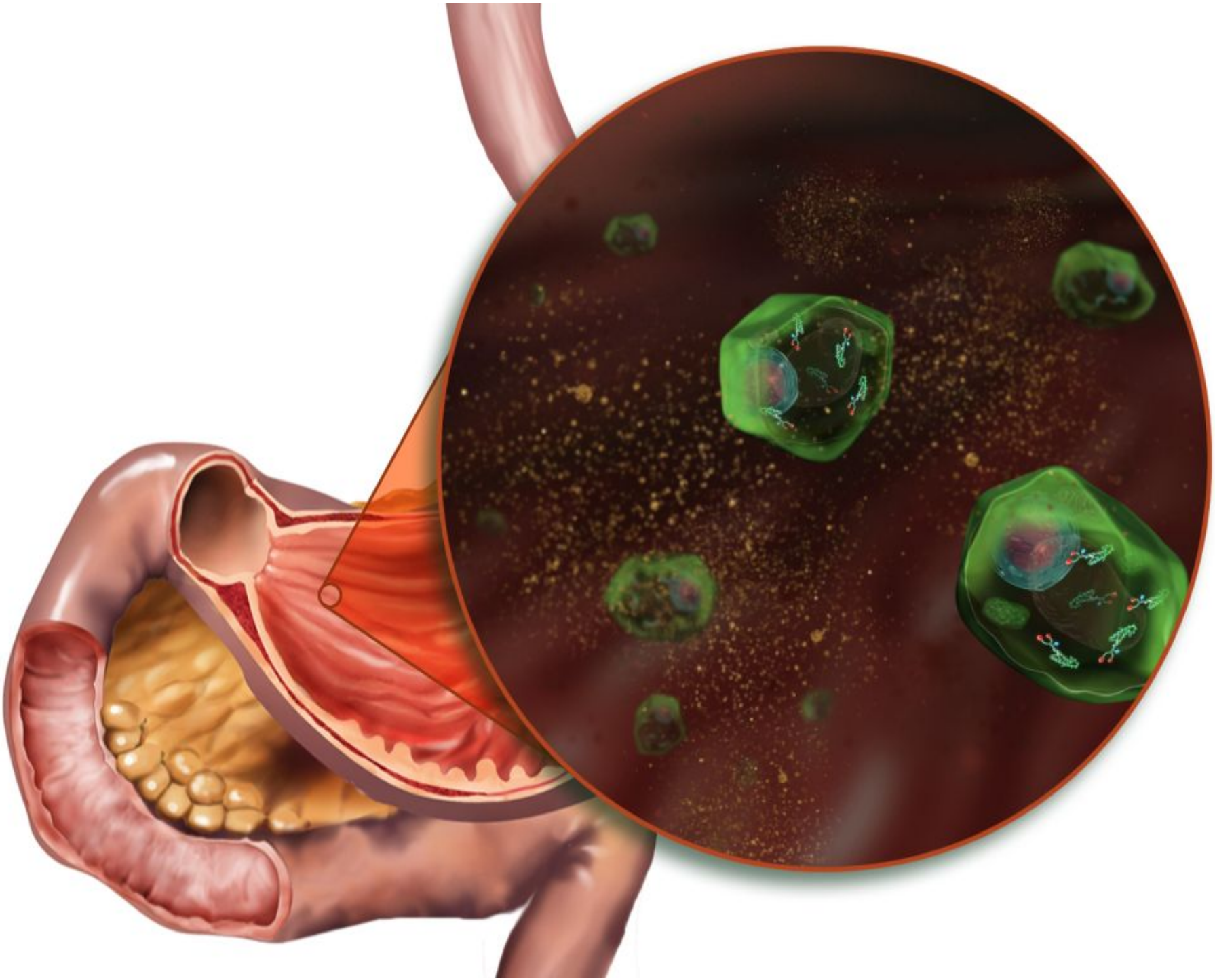
PRX-112: Plant expressed GCD for oral ERT

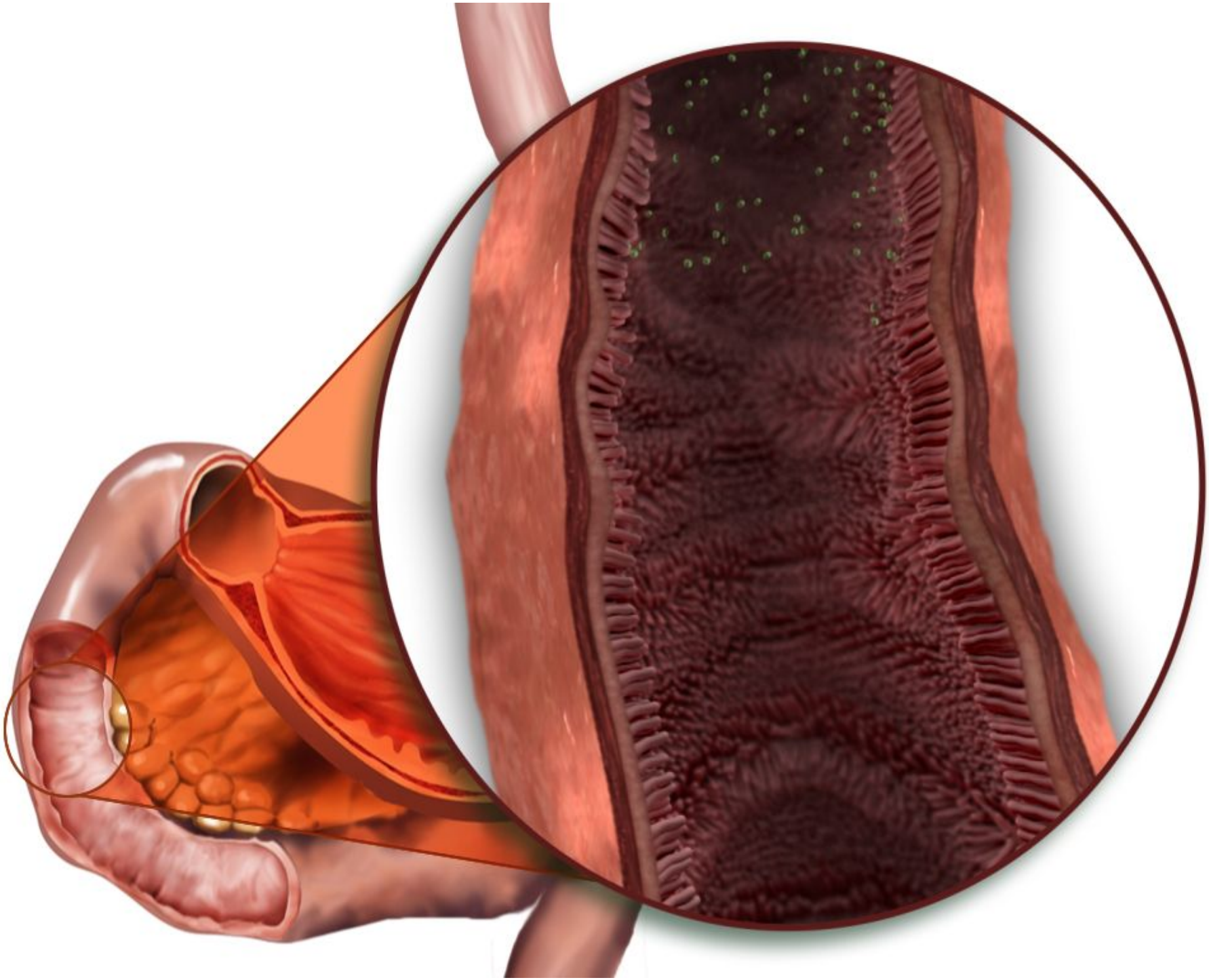
- Edible carrot cells expressing recombinant human glucocerebrosidase (prGCD)
- Same genetically modified carrot plant root cells from which the approved drug Elelyso™
- prGCD expressed in carrot cells as a "ready to use" enzyme
- Once in blood, the enzyme is expected to act like the approved IV administered Elelyso™
- PRX-112 carrot cells are prepared as a drink for "patient friendly" administration

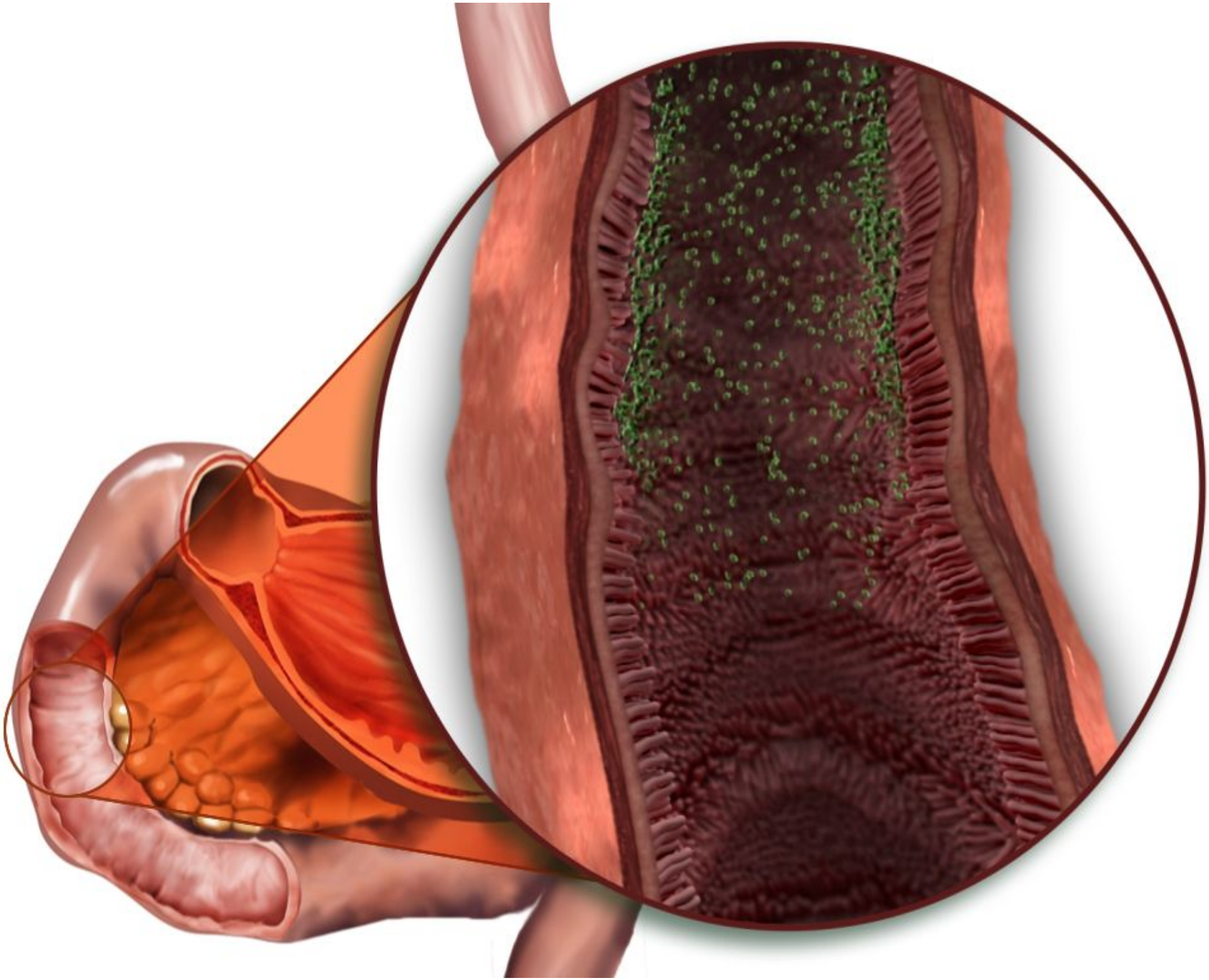


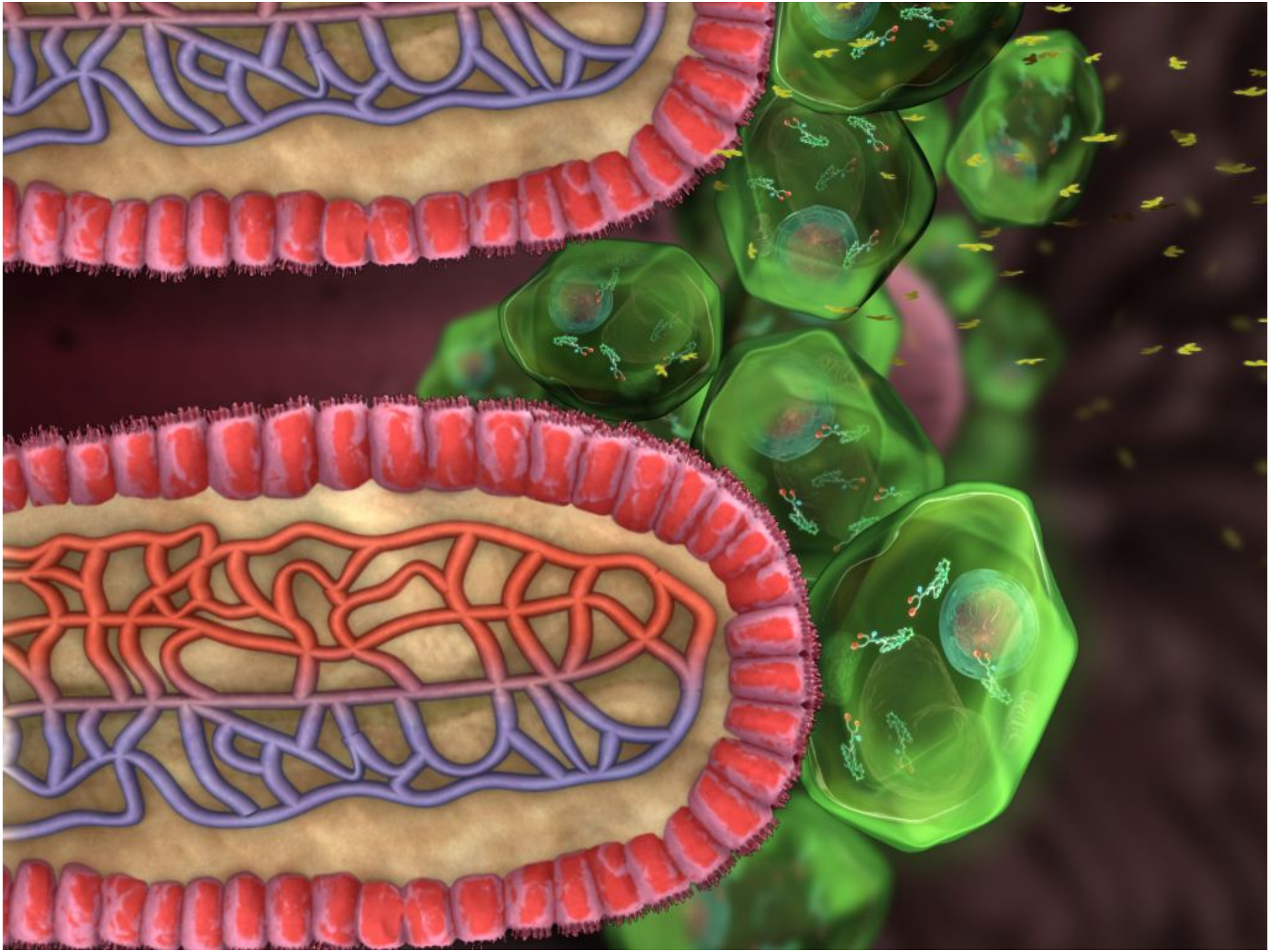


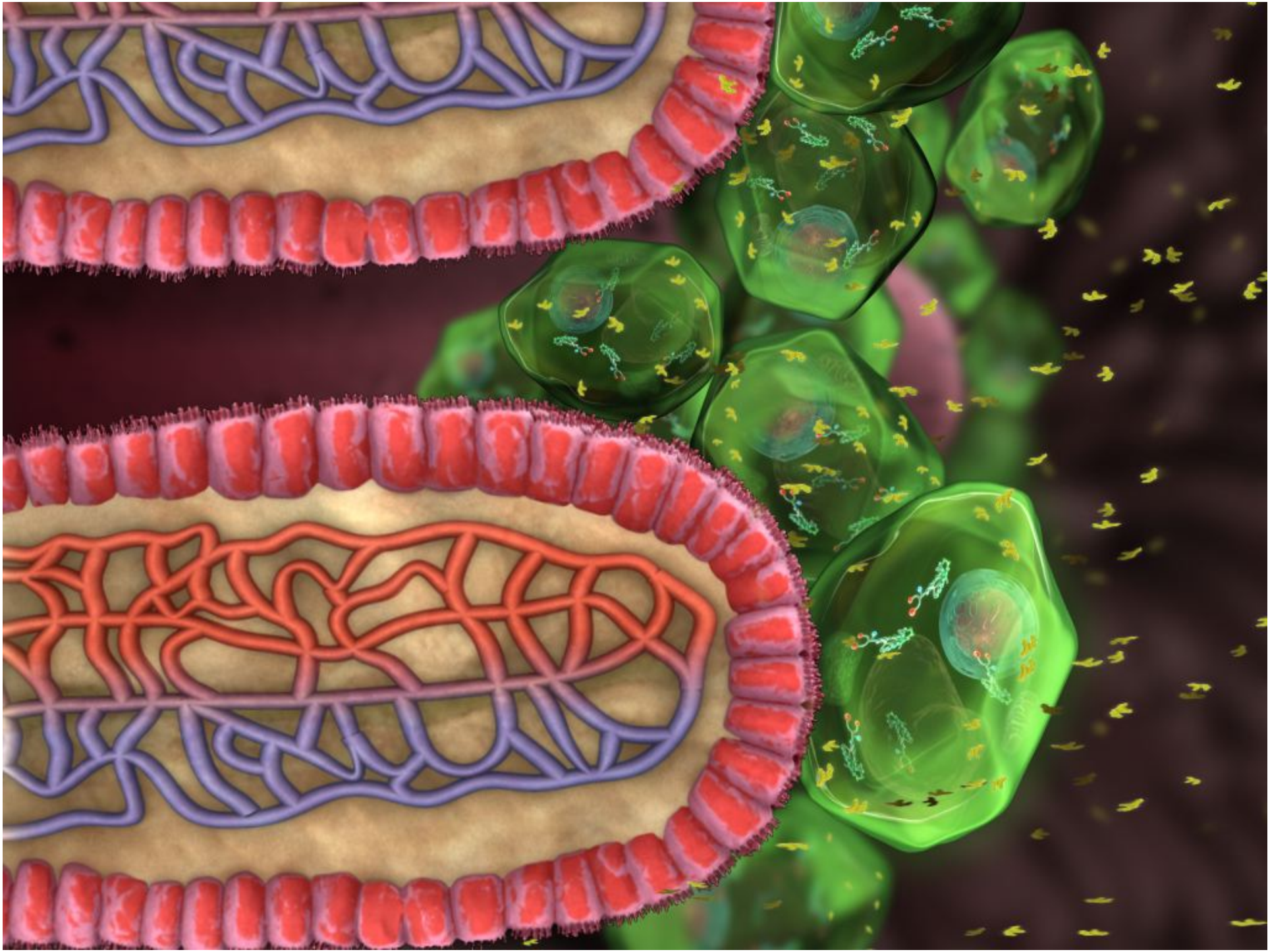


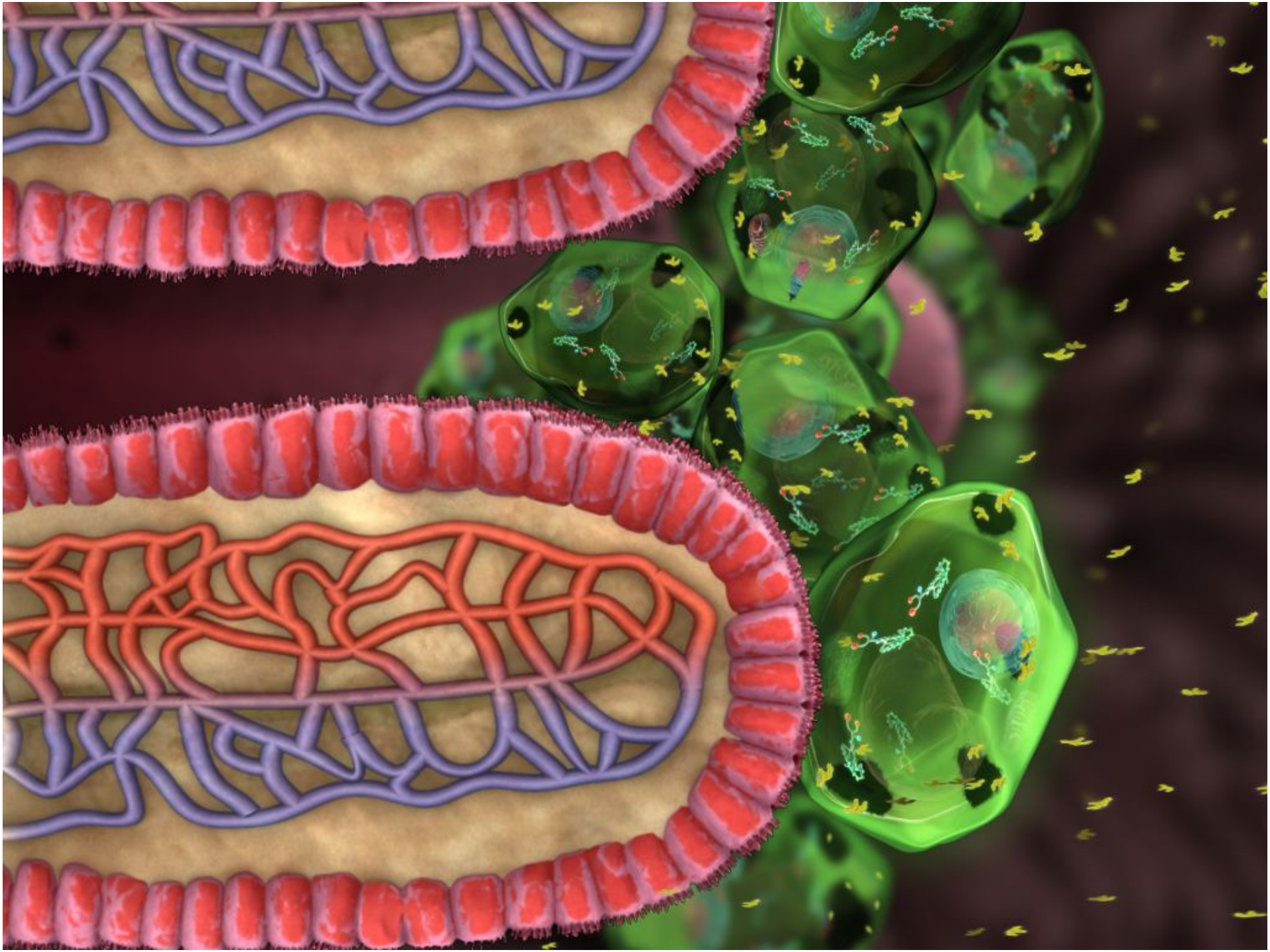


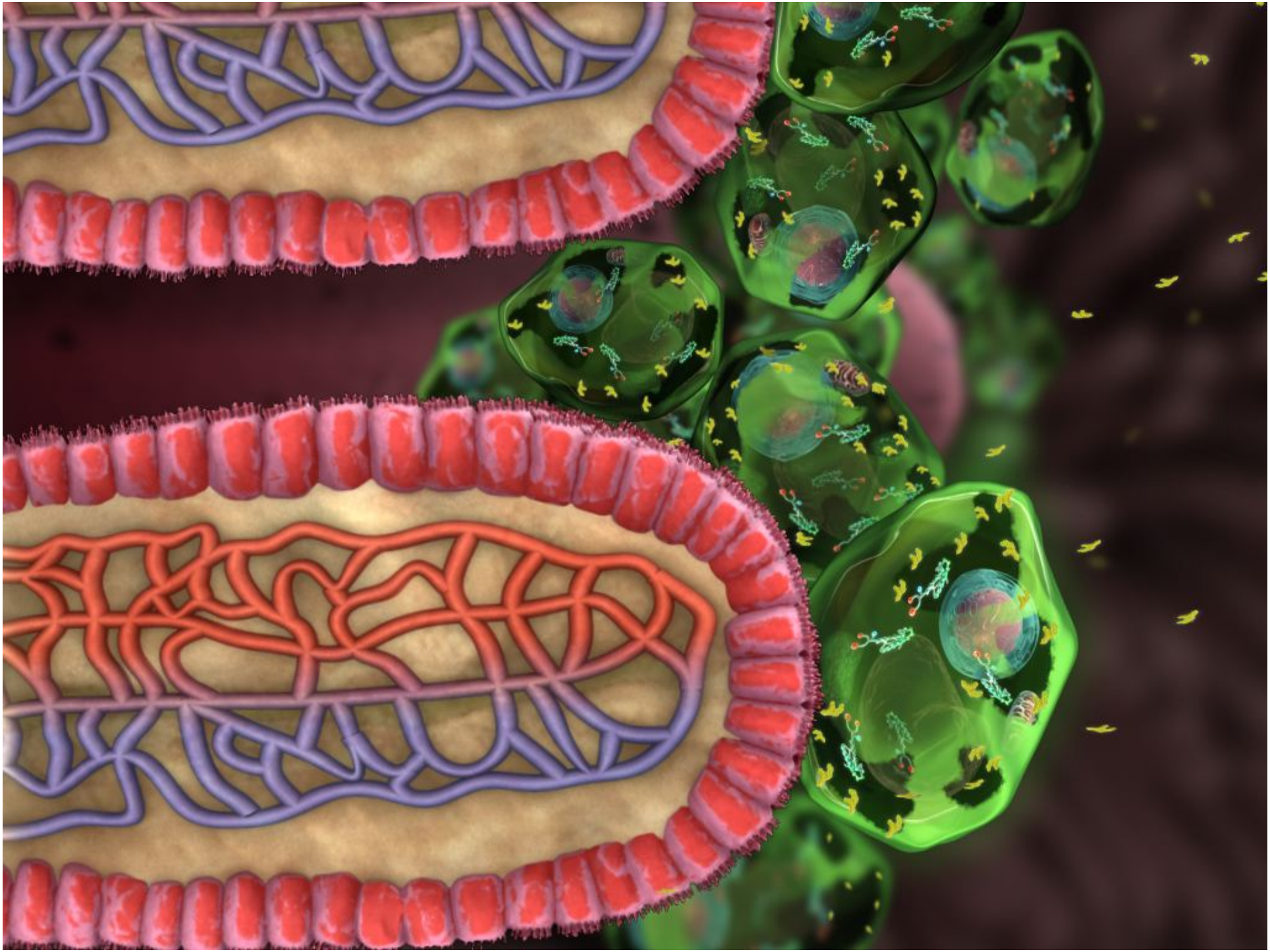


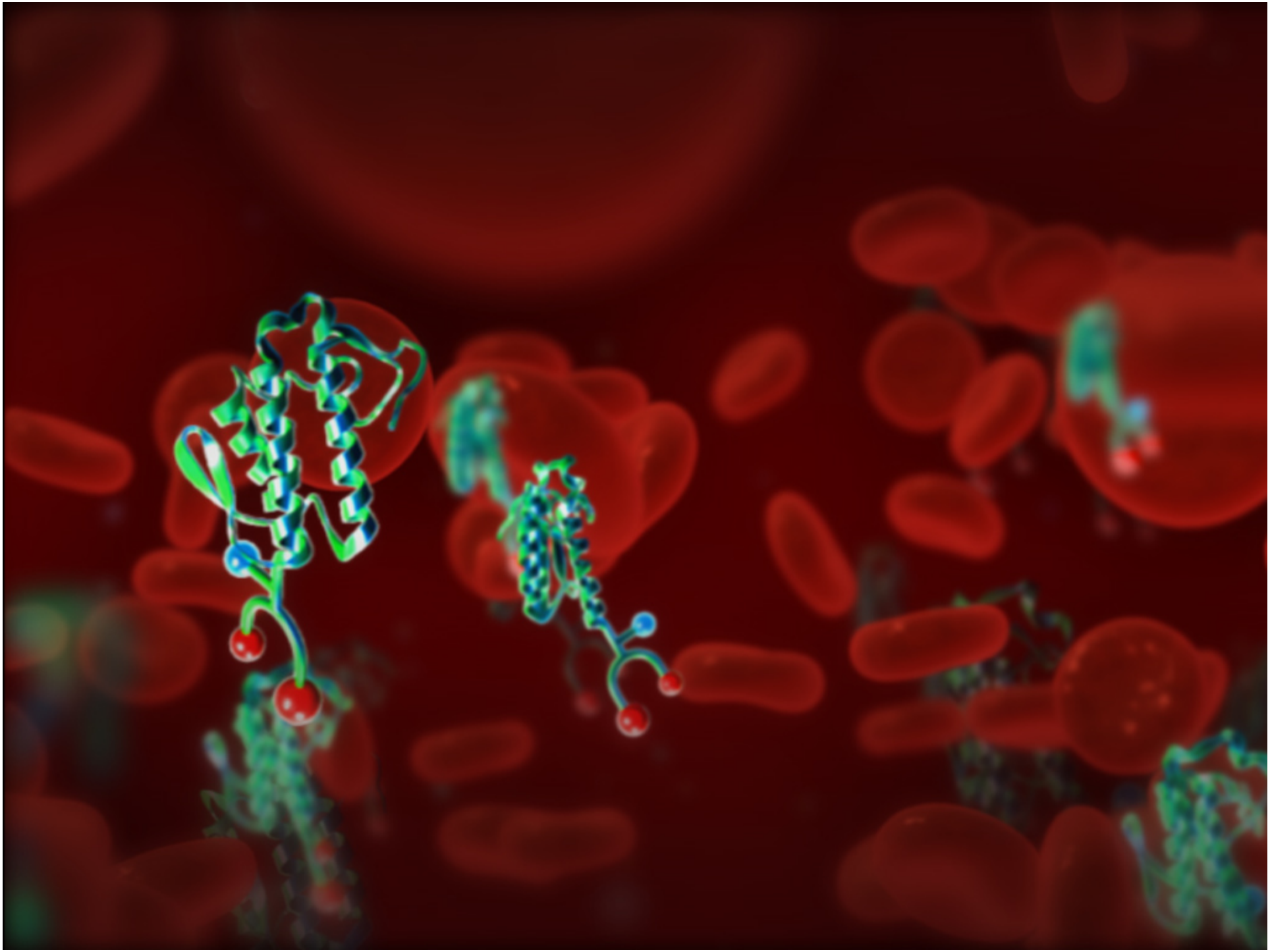


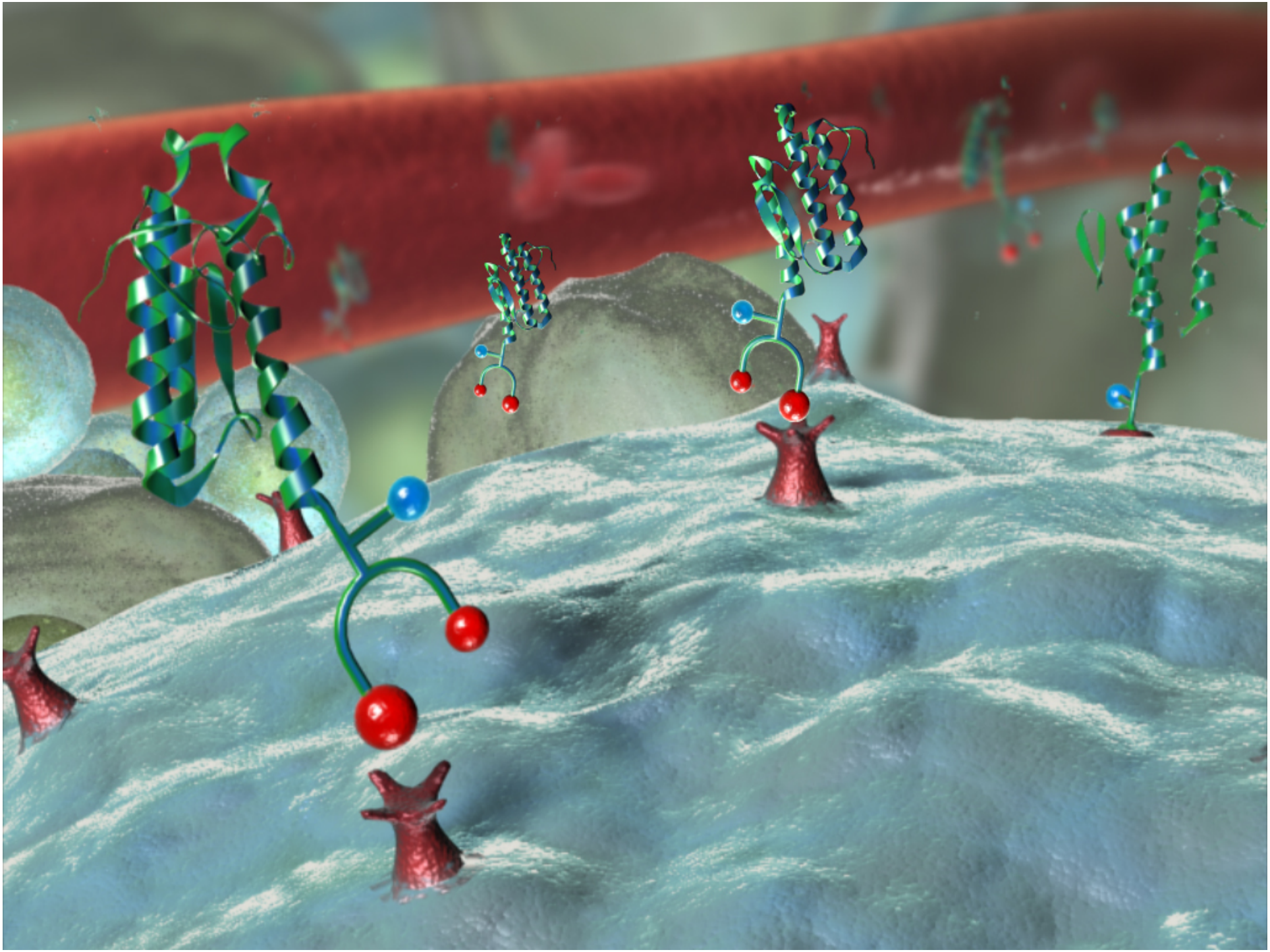












PRX-112 Phase I Study Design

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

- Adult Gaucher patients (12 in total; 6 males and 6 females)
- 3 sequential dose cohorts (2 males+2 females/cohort)
- PRX-112 cell suspension administered orally as follows:
  - **Treatment Period A**: Single administration followed by PK
  - **Treatment Period B**: 3 consecutive daily administrations at the same dose followed by PK after last dosing
- Dosing administered with controlled diet (until 2 hours after drug administration)

PRX-112 Phase I Study Design

Primary Objective:

– To assess the **safety** of oral administration of **PRX-112** in Gaucher patients

Secondary Objective:

– Determine the **PK of prGCD** in plasma of Gaucher patients after **PRX-112** oral administration

PRX-112 Phase 1 study strategy

Study aim:

Detection of prGCD in circulation after oral administration

Strategy:

- Evaluation of in of prGCD in plasma of untreated Gaucher patients
- Inclusion criteria - no detection of prGCD in plasma
- Collection of blood samples at short intervals over 30 hrs
- Assessment of prGCD in plasma at each time point
- Assessment of prGCD in circulating mononuclear white blood cells

PRX-112 Phase 1 study status

- Study conducted under Israeli MOH and IRBs approval
- Study initiated in Shaarei Zedek (Jerusalem) and Rambam (Haifa) medical centers
- 1st cohort (4 patients) – completed
- Expected Study completion – Q3 2013

1st cohort - Initial observations

- No drug related or any safety events
- Good compliance
- Detection of orally administered enzyme in the circulation

The Future

Oral Immune Therapy Using Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106)

Yaron Ilan, M.D.
Gastroenterology and Liver Units,
Department of Medicine
Hebrew University-Hadassah Medical Center
Jerusalem, Israel

6/2013

Forward Looking Statement

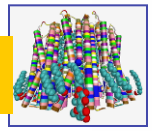
Please be advised that the information and projections provided in this presentation may include forward-looking statements with respect to plans, projections or future performance of PRX-106 and Protalix, the occurrence of which involves certain risks and uncertainties and is not under the control of the company, including, but not limited to, changes in regulatory environment and improving metabolic homeostasis, success in implementing its research, development, sales, marketing and manufacturing plans, protection and validity of patents and other intellectual property rights and the effect of competition by other companies.

Disclosure

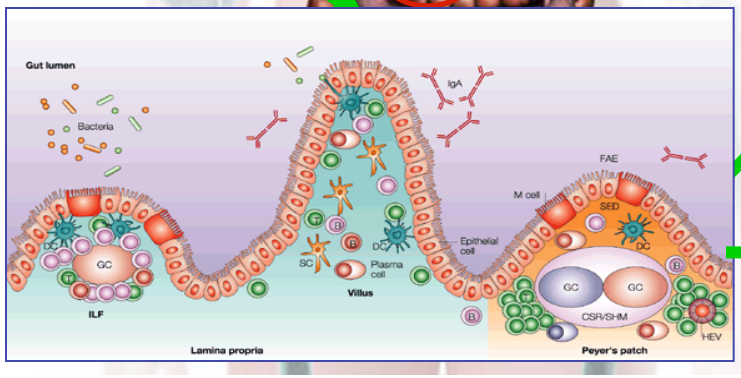
I have financial relationships with Protalix and the content of my presentation does include a discussion of the investigative use of PRX-106.

Oral Immune Therapy Using Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106)

PRX-106



Presented to the
Gut associated lymphoid tissue
& dendritic cells



Target organs
- Bowel
- Pancreas
- Adipose tissue
- Liver
- Brain

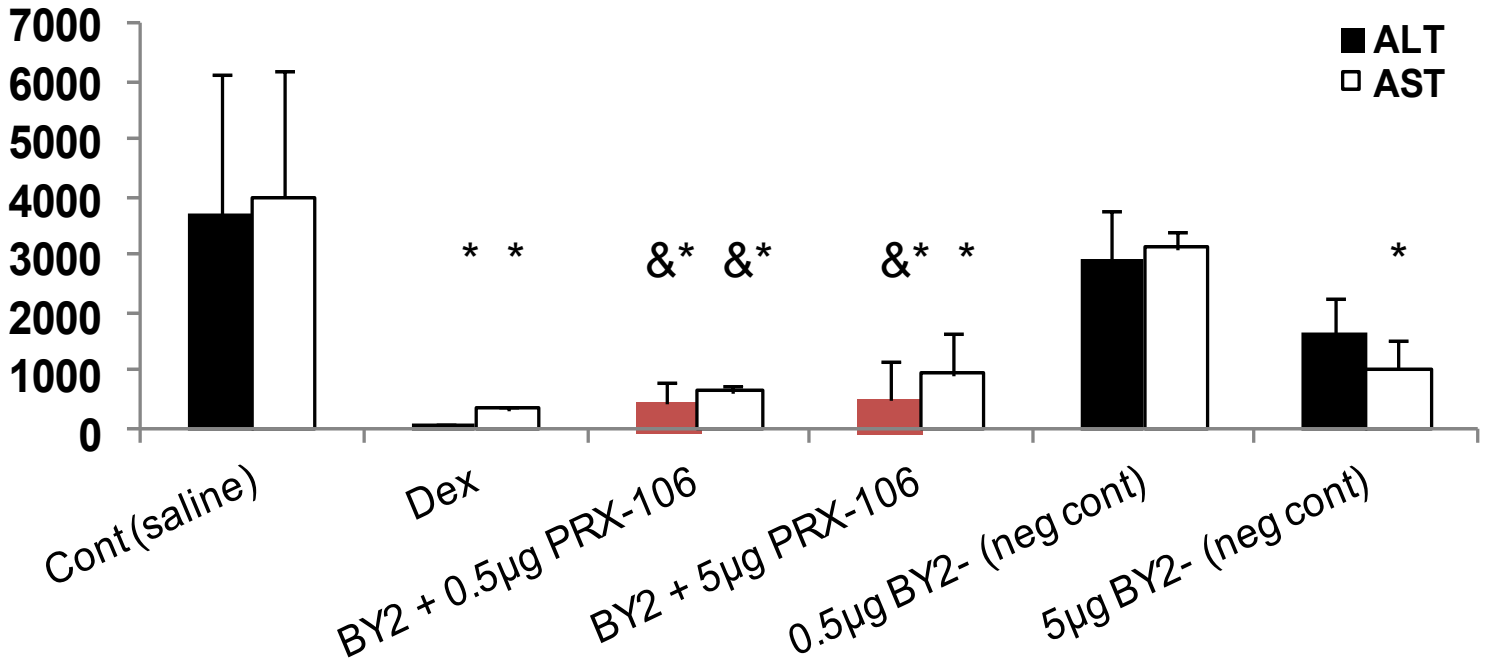
Induction of regulatory T cells (Tregs) in mesenteric lymph nodes

A potential direct effect following absorption

Modified from: Ilan Y, Immunology Cell Biology, 2009

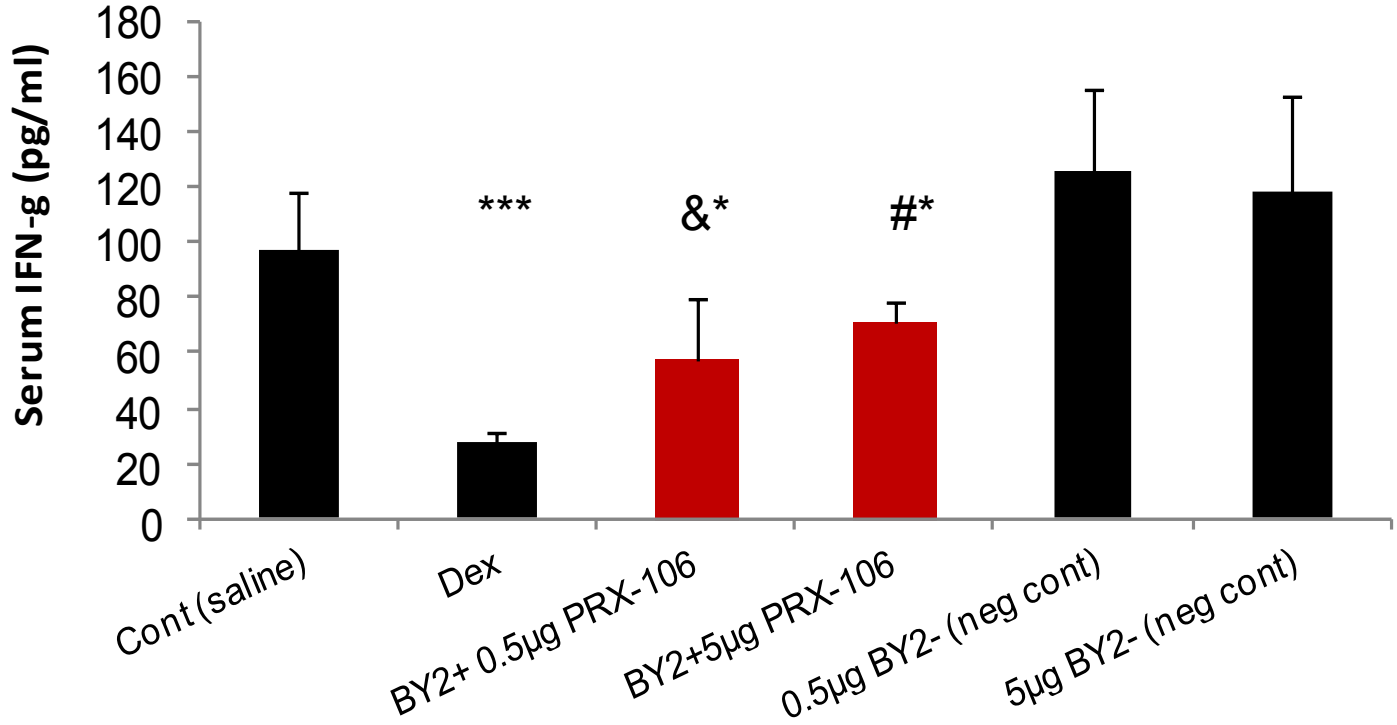
Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Alleviates Immune-mediated Hepatitis

Orally Administered Plant Cell-expressed Recombinant Anti-TNF fusion protein (PRX-106) Alleviates ConA Immune-Mediated Hepatitis



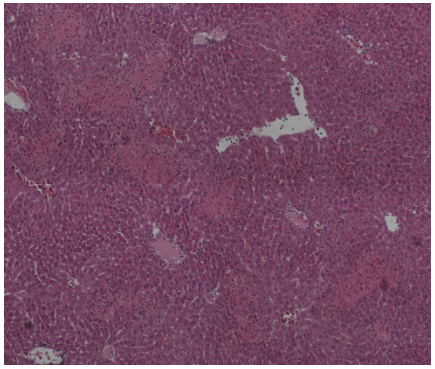
* p<0.02; relative to saline; & p< 0.0005, relative to negative control
# p< 0.03, relative to negative control

Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Reduces IFNγ Serum Levels

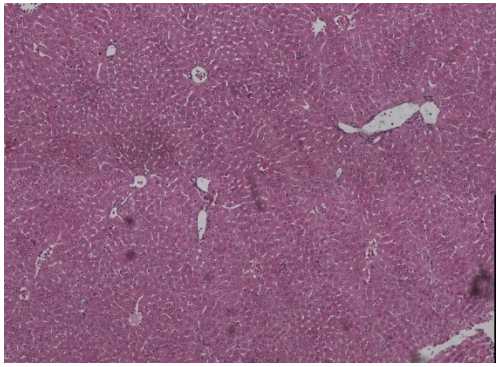


* p<0.05; ** p<0.00001, relative to saline; & p< 0.004, relative to negative control
# p< 0.02, relative to negative control

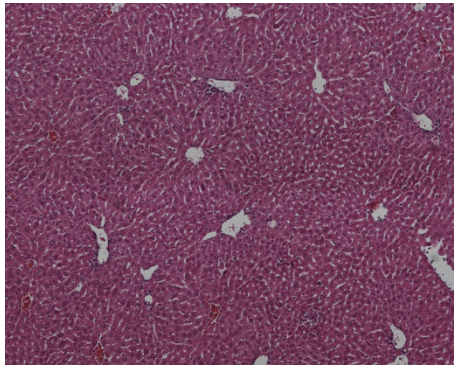
Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Alleviates ConA Immune-mediated Hepatitis



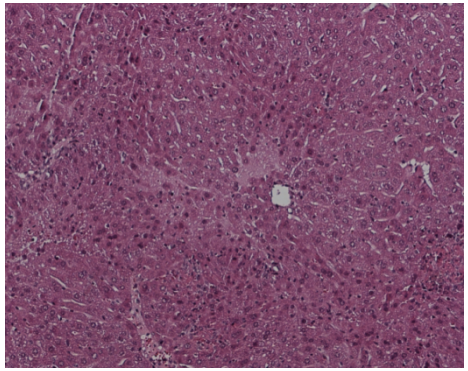
ConA,
Control (saline)



ConA,
Dex



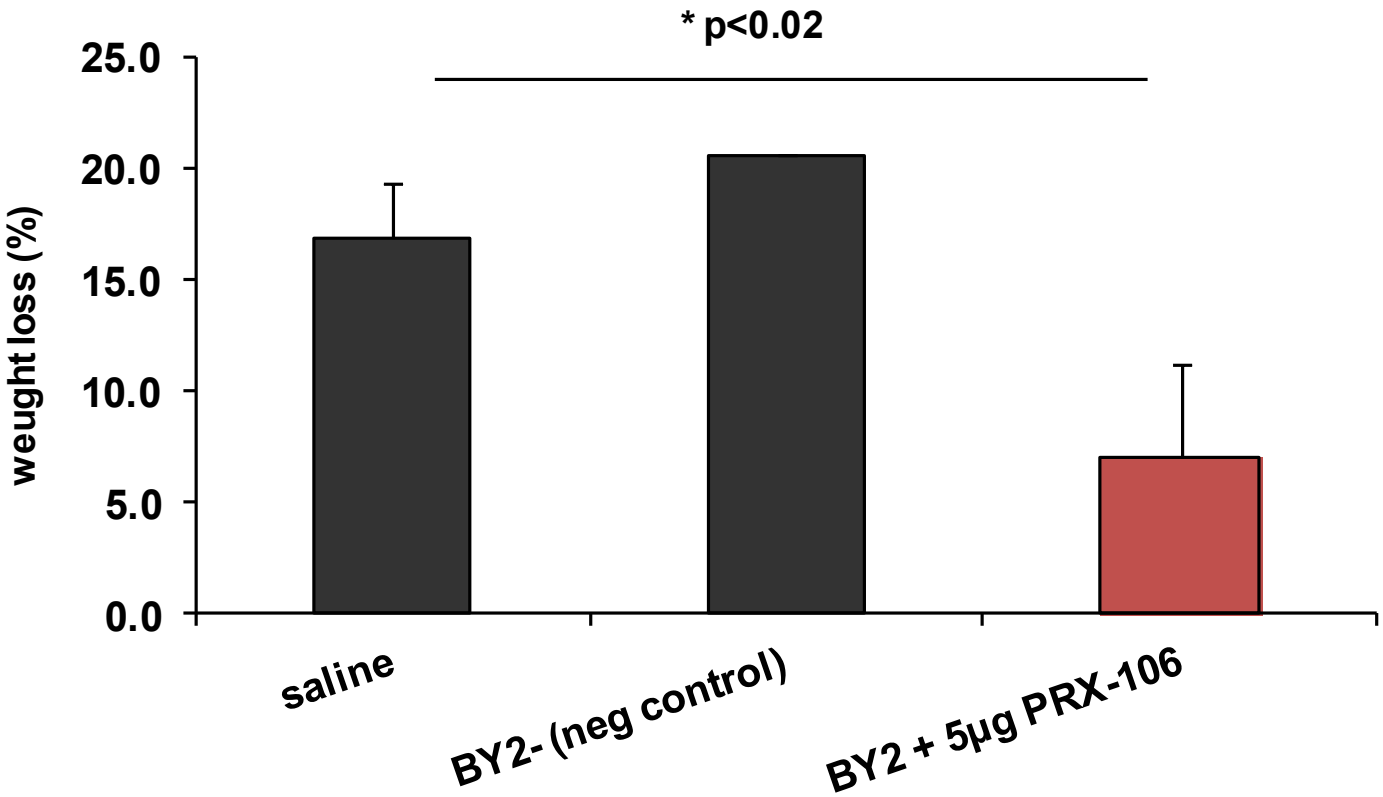
ConA,
0.5μg PRX-106



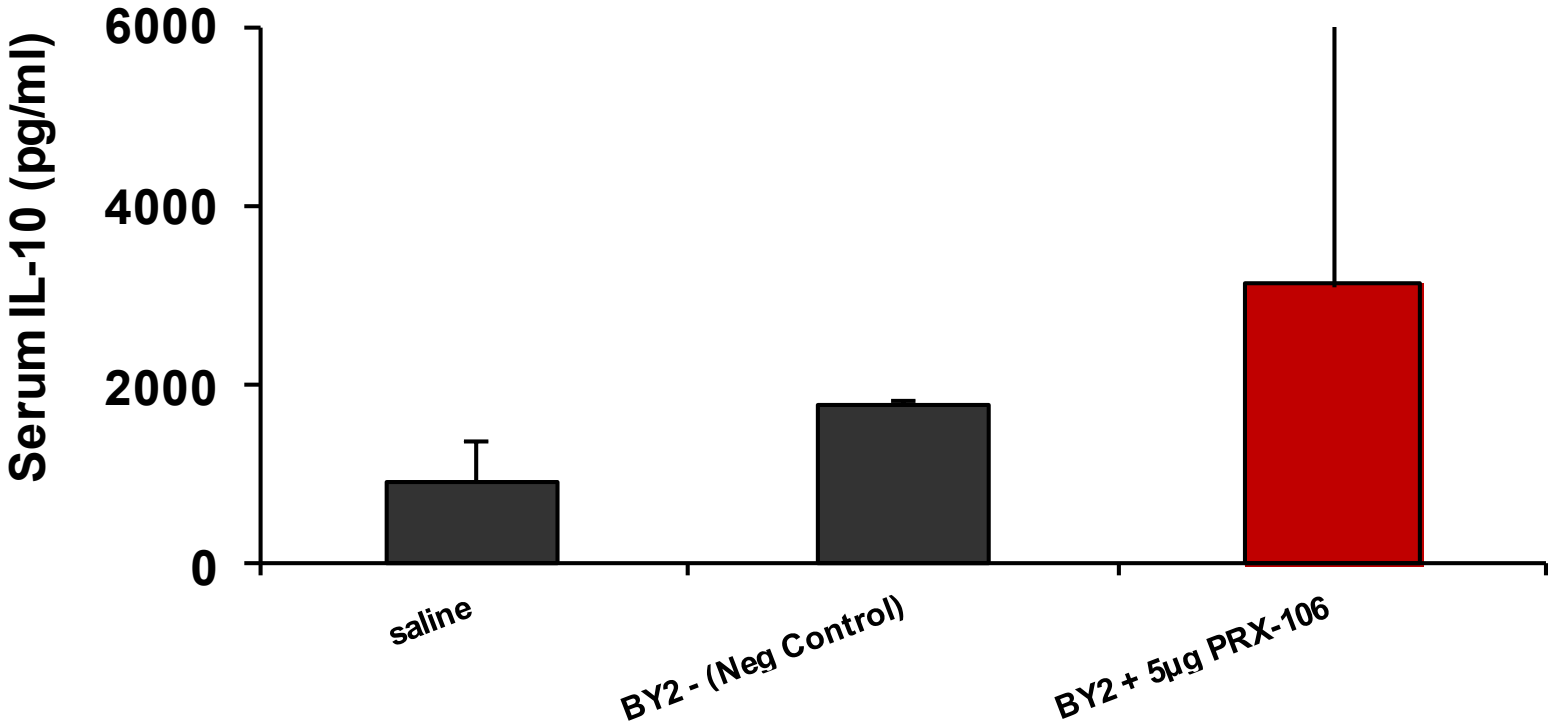
ConA,
0.5μg BY2
(negative cont)

Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Alleviates Immune-mediated Colitis

Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Alleviates Immune-mediated Colitis

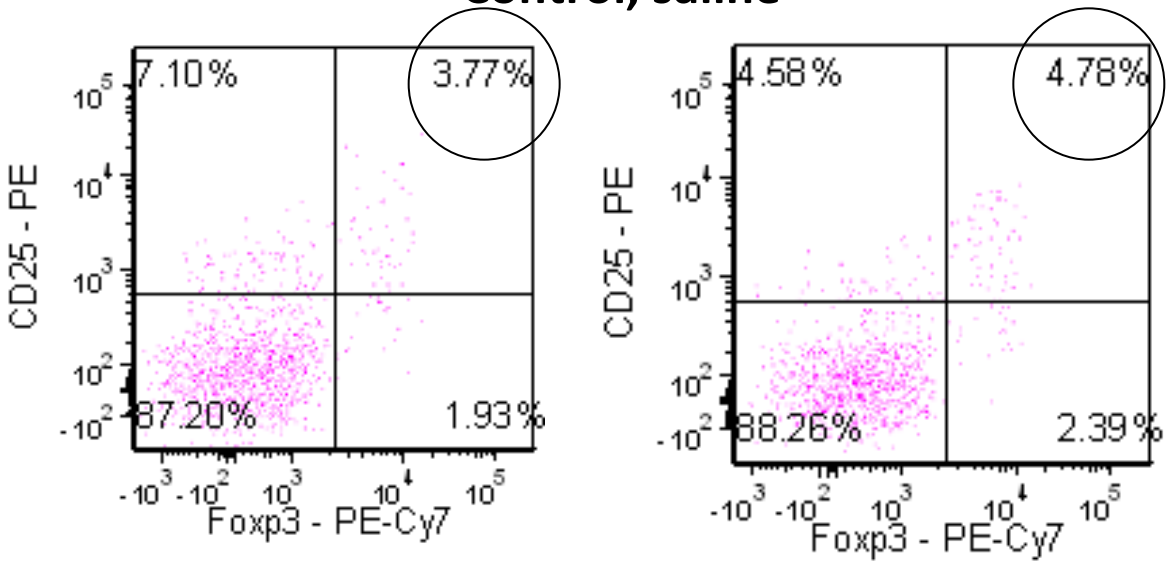


Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Promotes Serum Levels of Anti Inflammatory IL-10

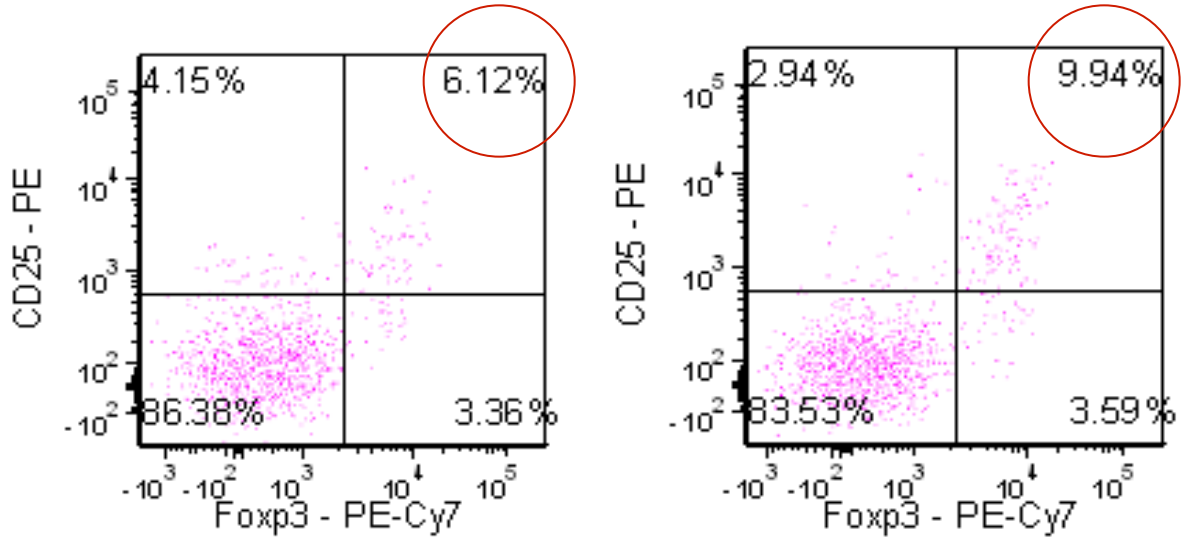


Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) Promotes Intrahepatic CD4+CD25+FoxP3+ Tregs

Control, saline



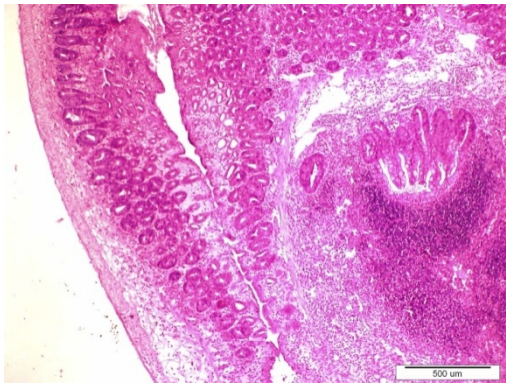
BY2 + 5µg PRX-106



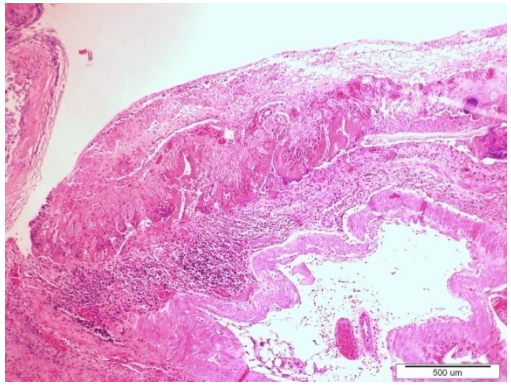
Summary

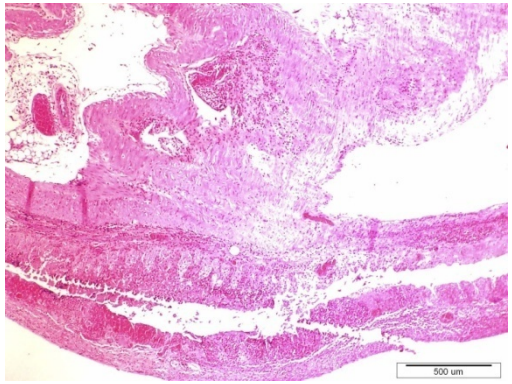
A1	3.77	**C1**	9.35
A2	4.78	**C2**	6.12
A3	5.32	**C3**	9.94

Saline

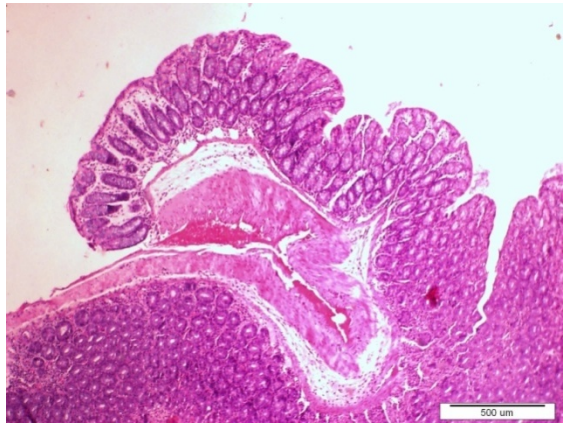


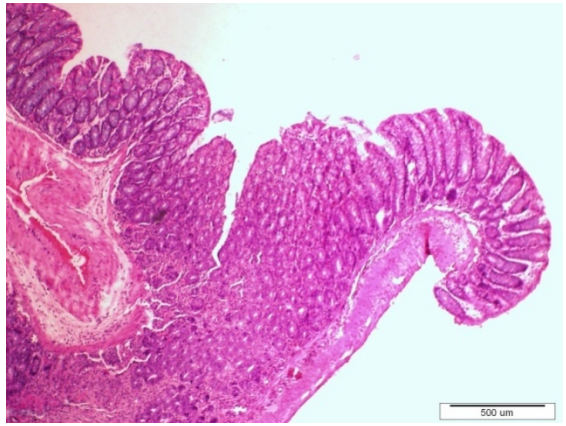
0.5μg BY2- (Negative control)





BY2+ 0.5μg PRX-106





Orally Administered Plant Cell-expressed Recombinant Anti-TNF Fusion Protein (PRX-106) For Diabetes, Hyperlipidemia And Fatty Liver Disease

Obesity = low grade chronic inflammation

The metabolic syndrome

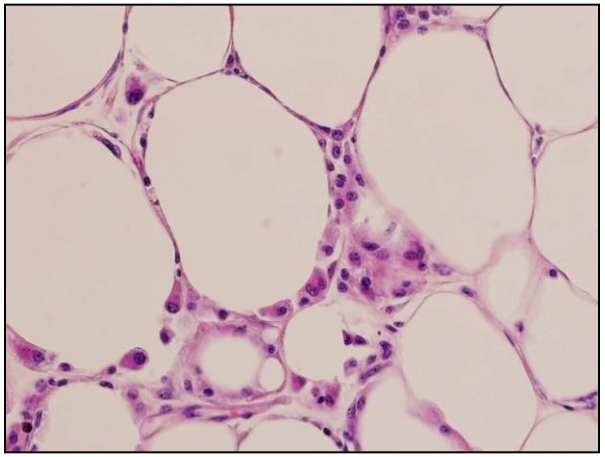
Diabetes type 2

Fatty liver disease

Atherosclerosis

Hyperlipidemia

Projection: Within 20 years, 50% of the world population will suffer from the metabolic syndrome.



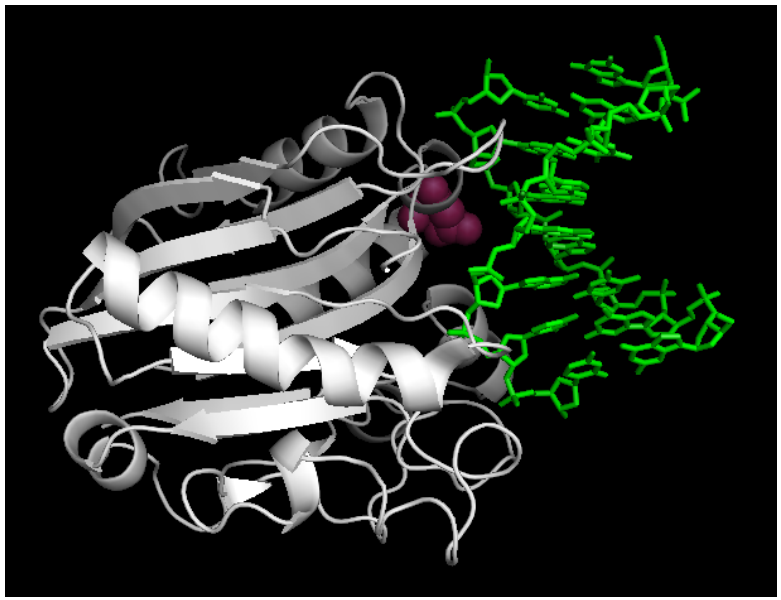
PROTALIX Biotherapeutics

Thank you

PRX-110 & PRX-107

Dr. Yoseph Shaaltiel, Executive Vice President,
Research and Development, Protalix

PRX-110 – Plant Cell Recombinant Deoxyribonuclease I (DNase I) for the Treatment of Cystic Fibrosis



DNase I

- **Protein:** Recombinant human deoxyribonuclease
- **Indication**: Cystic Fibrosis (CF)
- **Protein function:** Break down of excessive DNA in the accumulated mucus (sputum) in lungs of CF patients decreases viscosity of airway secretions
- **Market (2012):** 572M$
- **Marketed Product**: Pulmozyme (Roche; Genentech)
- **IP-** Product patents expiration date: 2013

PRX-110 Product Description

PRX-110 Advantages:

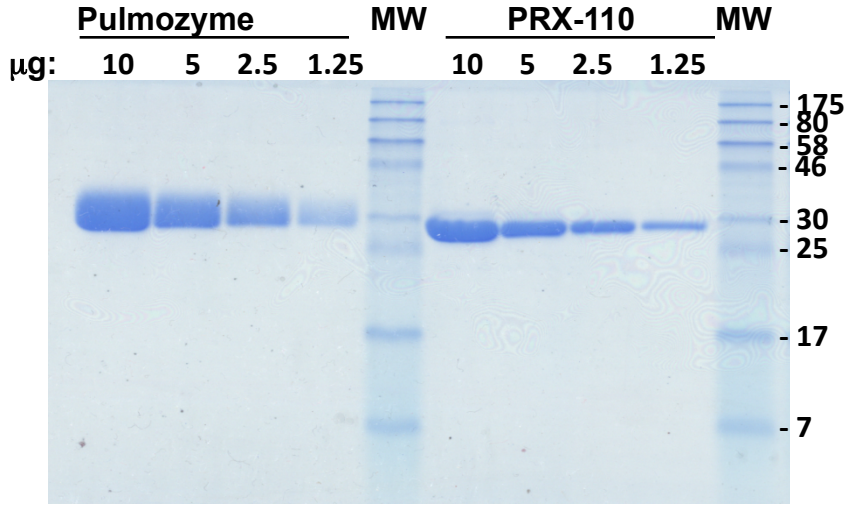
- Improved enzyme kinetics
- Less sensitive to inhibition by actin
- Improved ex-vivo efficacy

PRX-110 properties can potentially lead to:

- Different regimen
- Lower cost

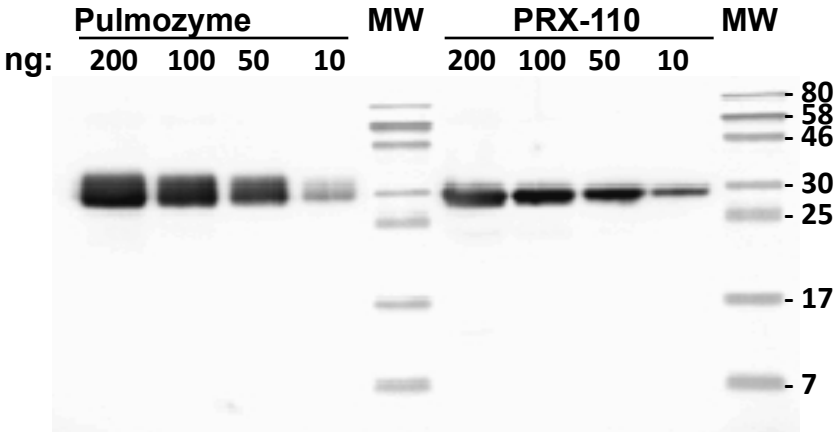
PRX-110 Characterization

SDS-PAGE



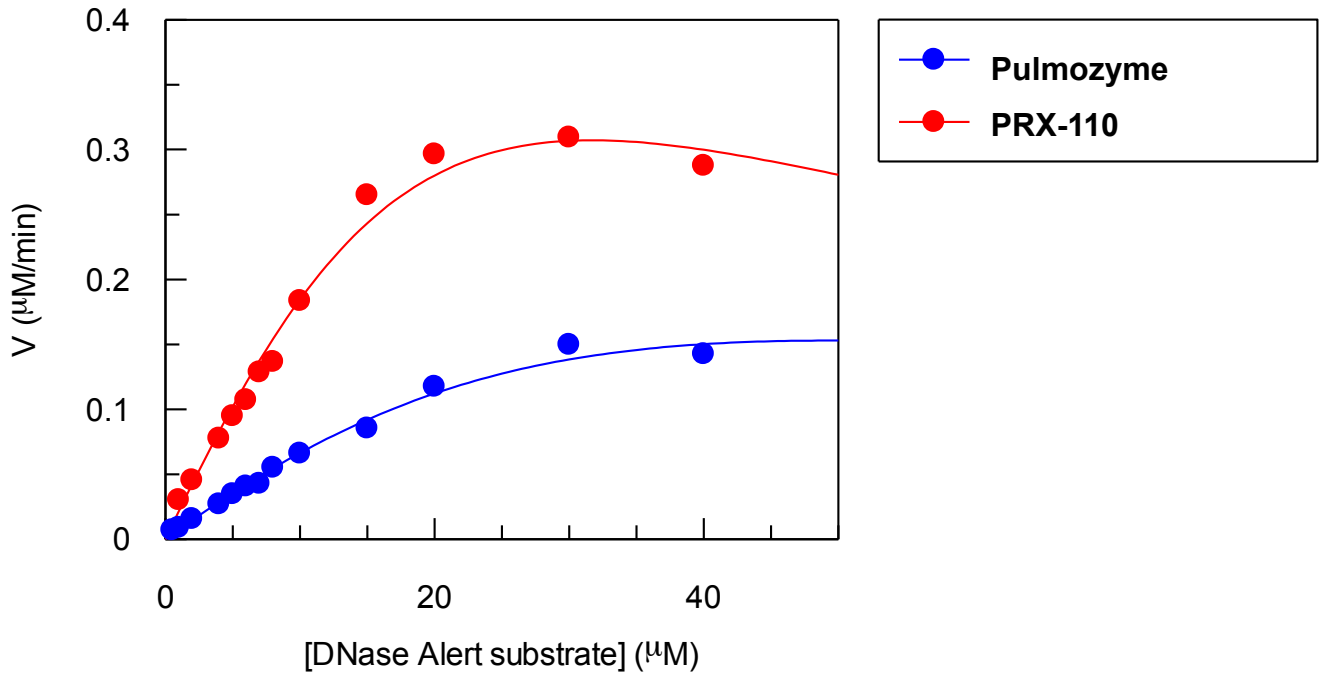
Western blot

Anti Pulmozyme Ab



Improved Enzyme Kinetics

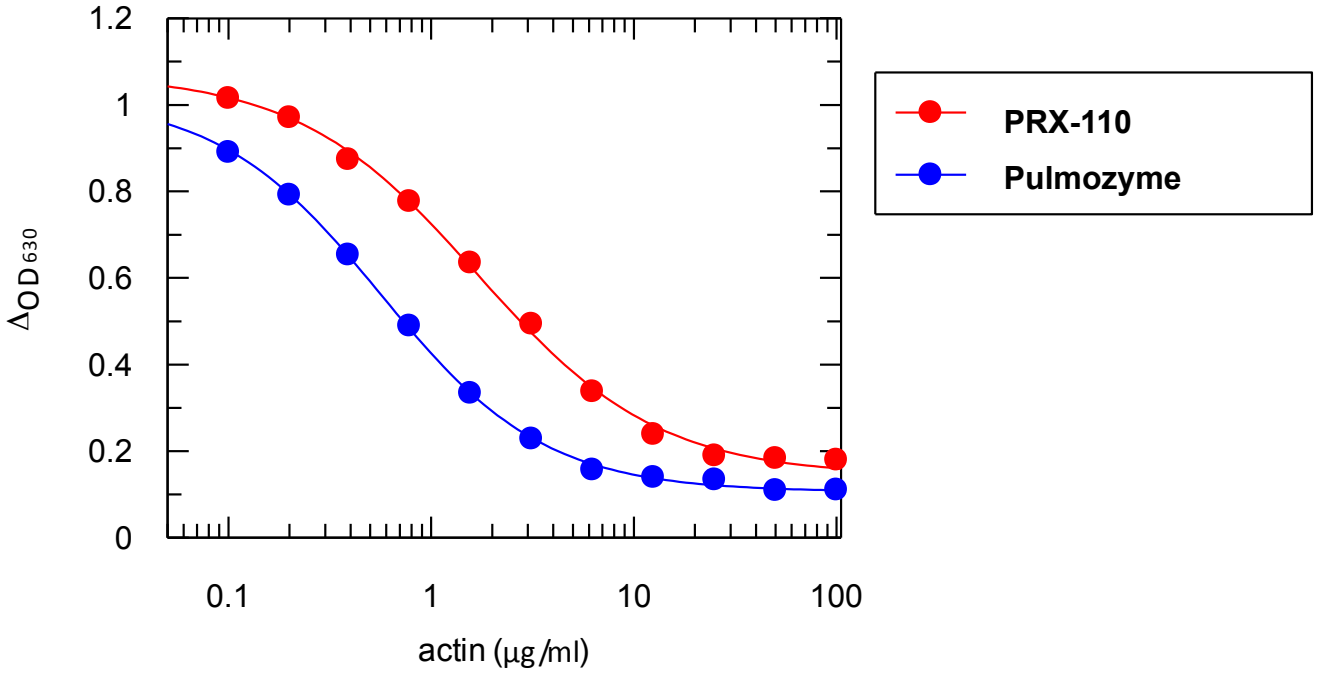
PRX-110 vs. Pulmozyme



DNase I	K_M (μM)	V_{max} (μM/min)	k_{cat} (sec^{-1})	k_{cat}/K_M ($sec^{-1}\mu M^{-1}$)
PRX-110	24.3	0.58	6.24	0.26
Pulmozyme	60.9	0.44	4.76	0.08

Reduced Inhibition of PRX-110 by human actin (IC_{50})

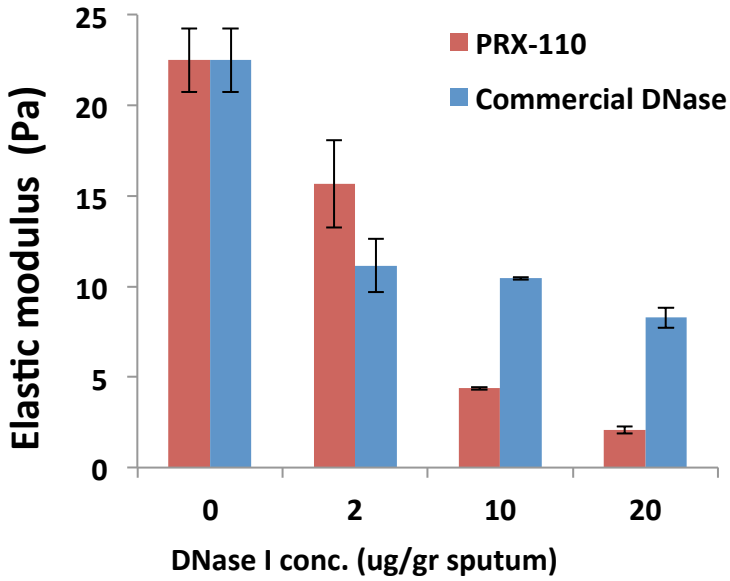
PRX-110 vs. Pulmozyme

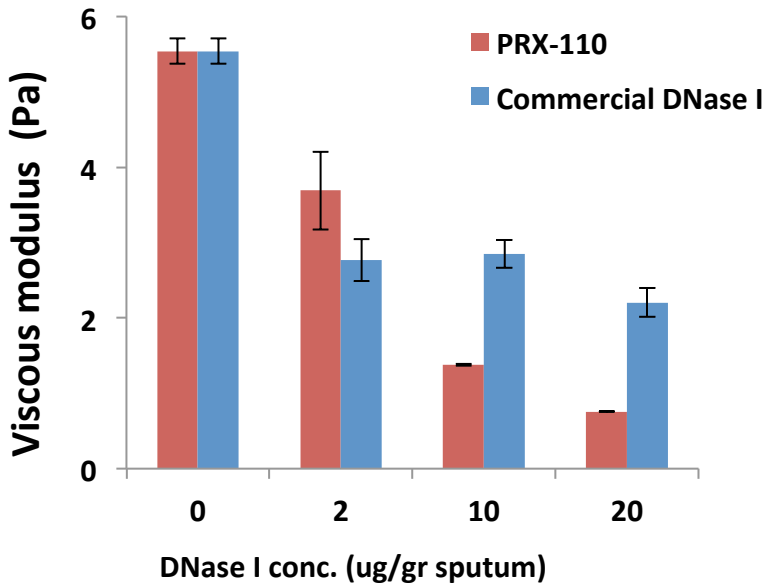


DNase I	Actin (ug/ml)
PRX-110	1.8191 ± 0.1003
Pulmozyme	0.6870 ± 0.0204

Ex-vivo Efficacy Study on CF Patient's Sputum

PRX-110 vs. Pulmozyme

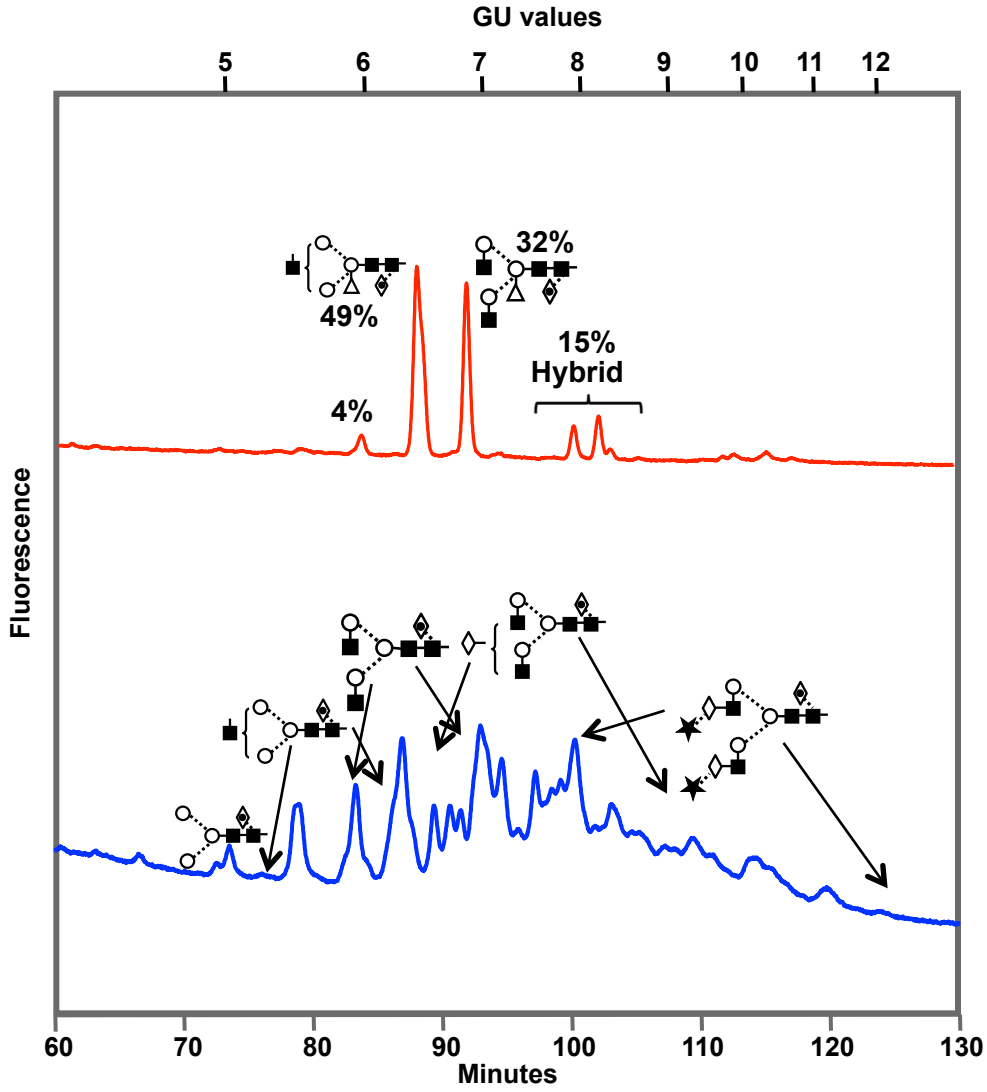




Improved Dose Dependent Effect of PRX-110 on the Rheological Properties of Sputum from CF Patients

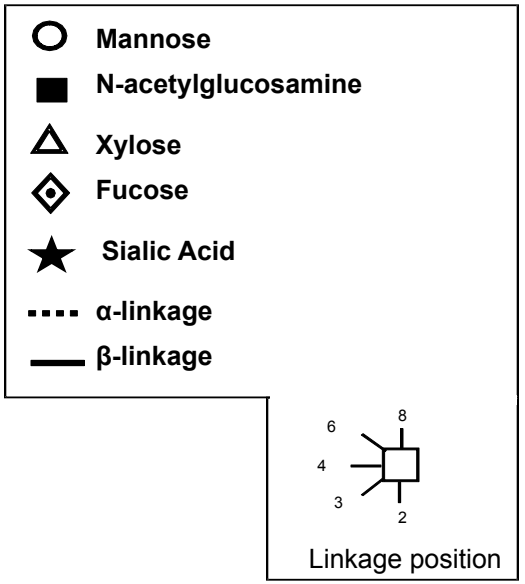
N-linked Glycosylation of DNase I

PRX-110 vs. Pulmozyme



PRX-110

Pulmozyme



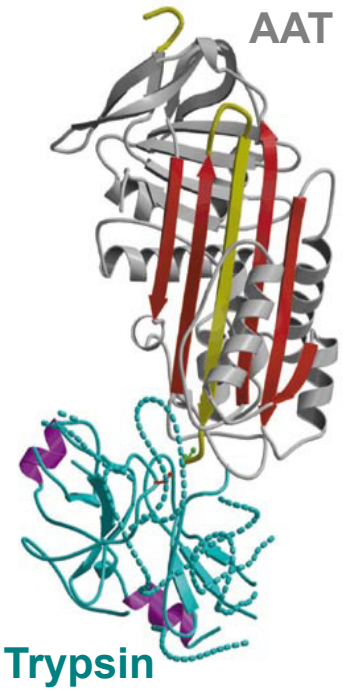
In Vivo Study - Inhalation of PRX-110 in Rats

- Nose-only aerosol inhalation exposure
- PRX-110 enzyme activity in animal lung after inhalation maintained substantial enzymatic activity

PRX-110 Development Status

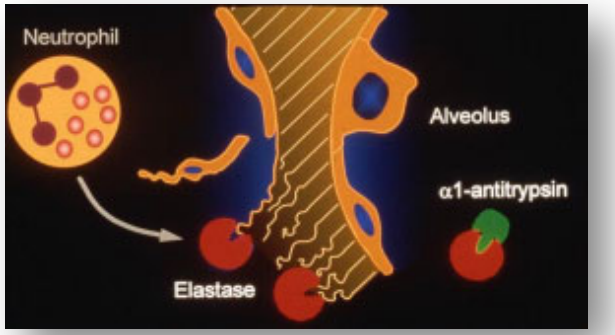
- pre-IND meeting held with the FDA
- Toxicity studies planned for Q4/2013

PRX-107 – Plant Cell Recombinant Human Alpha1-antitrypsin (AAT) for the Treatment of Pulmonary Disorders



Alpha1-antitrypsin (AAT)

- Main function: regulates AAT-dependent inflammatory response in the lungs
- Single-chain protein: 394aa, 52kDa
- Indication: Emphysema due to Hereditary AAT deficiency (AATD)
- Market (2012): est. ~$600M
- Marketed products are purified from plasma and administered IV
- **No recombinant AAT approved**



PRX-107 (AAT) Advantages

All marketed AAT products are plasma-derived

- Limited plasma supply
- Potential adventitious agents

Protalix benefit: Recombinant AAT

- Easy scale up to meet demand
- No potential adventitious agents
- Lower production cost

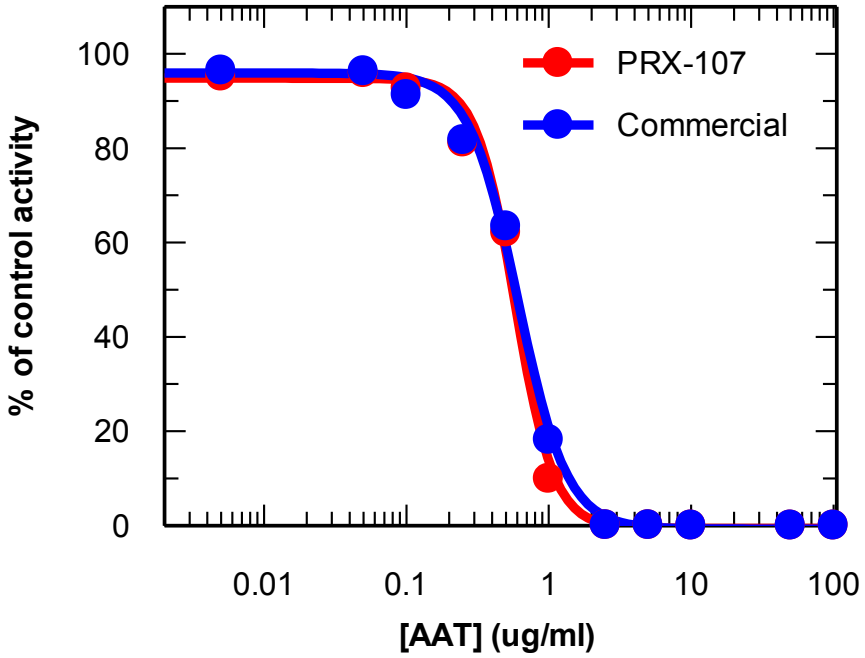
All marketed products are for IV use

- IV delivery results in only ~2% of the protein reaching the lungs

PRX-107 goal: Inhalation delivery

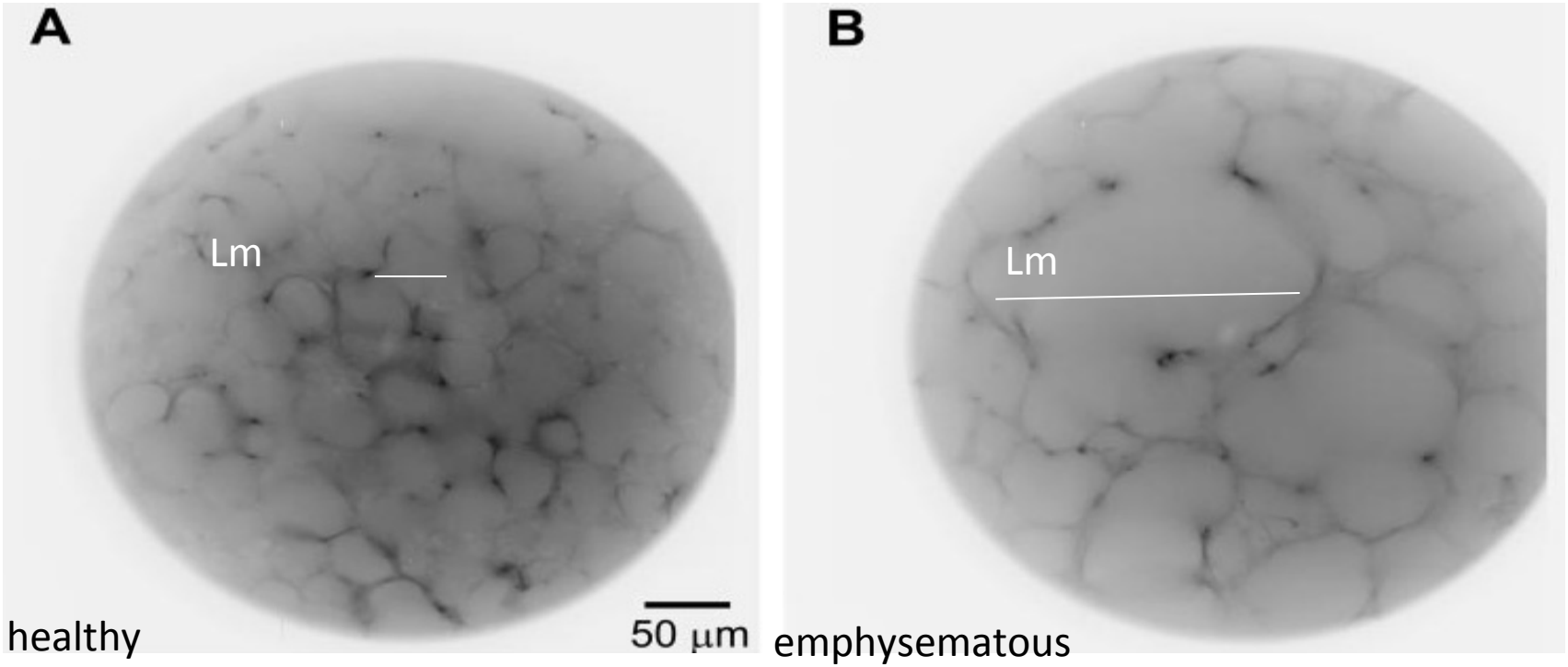
- Directly to the lungs
- Better patient quality of life

Biological Activity – IC_{50}



Similar amounts of PRX-107 and commercial AAT reagent needed to achieve 50% inhibition of Elastase

In vivo Induced Emphysema Model



healthy

emphysematous

Lm – mean linear intercept (diameter)
V_L – lung volume
Sa – alveolar surface

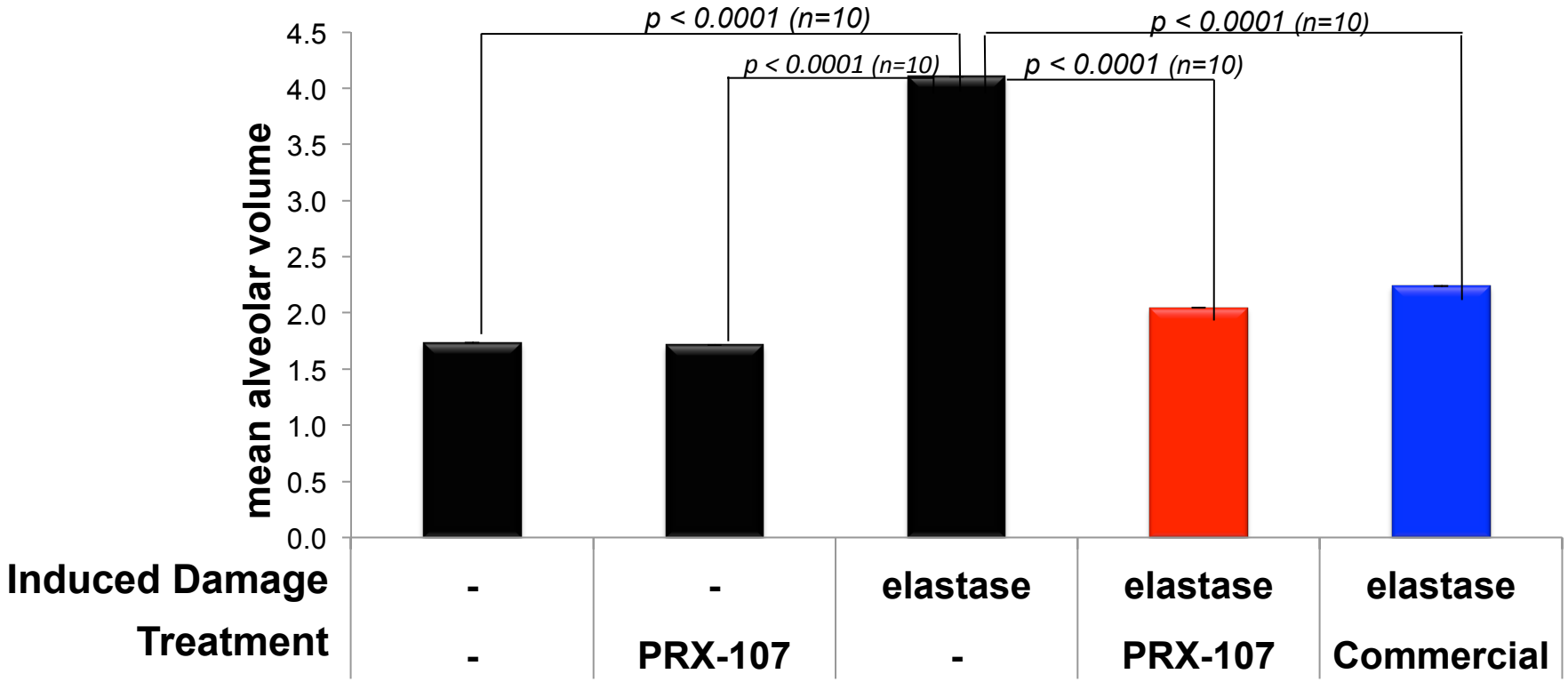
PRX-107 *In-vivo* Efficacy Study in Rats

Group ID (10 rats/group)	AAT (10mg/kg)	Elastase dose (U/g BW)
1	mock	0
2	PRX-107	0
3	mock	0.25
4	PRX-107	0.25
5	Commercial	0.25

Post-mortem analyses:

Efficacy *In-vivo* Study Results

- Experiment - AAT Ability to rescue Elastase induced lung damage
- Comparison between **PRX-107** and AAT (**plasma derived reagent)**
- The extent of the damage is measured by the mean alveolar volume



PRX-107 Development Status

- pre-IND meeting planned for H2 2013

Q&A Session