Amicus Therapeutics

Cowen and Company
33rd Annual Health Care Conference

John F. Crowley
Chairman & CEO

At the Forefront of Therapies for Rare and Orphan Diseases™

March 4, 2013

Safe Harbor

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 relating to business, operations and financial conditions of Amicus including but not limited to preclinical and clinical development of Amicus’ candidate drug products, the timing and reporting of results from clinical trials evaluating Amicus’ candidate drug products. Words such as, but not limited to, “look forward to,” “believe,” “expect,” “anticipate,” “estimate,” “intend,” “plan,” “would,” “should” and “could,” and similar expressions or words, identify forward-looking statements. Although Amicus believes the expectations reflected in such forward-looking statements are based upon reasonable assumptions, there can be no assurance that its expectations will be realized. Actual results could differ materially from those projected in Amicus’ forward-looking statements due to numerous known and unknown risks and uncertainties, including the “Risk Factors” described in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2012. All forward-looking statements are qualified in their entirety by this cautionary statement, and Amicus undertakes no obligation to revise or update this presentation to reflect events or circumstances after the date hereof.

Company Mission

Amicus Therapeutics is a biopharmaceutical company at the forefront of developing next-generation medicines to treat a range of rare and orphan diseases, with a focus on improved therapies for Lysosomal Storage Disorders

2013 Investment Highlights

Amicus Therapeutics

PRODUCTS

CHART™ CHAPERONE-ADVANCED REPLACEMENT THERAPY **PLATFORM**

PARTNERSHIPS

gsk GlaxoSmithKline

JCR Pharmaceuticals Co., Ltd.

LAUREATE BIOPHARMA

FINANCIAL STRENGTH

Core Technology and Focus

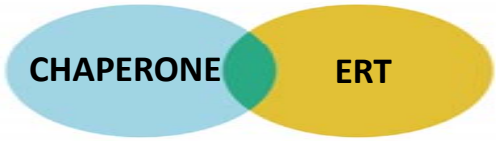
Potential to Transform LSD Treatments

Small Molecule Pharmacological Chaperones

ORAL CHAPERONE MONOTHERAPY

CHART™

CHAPERONE-ADVANCED REPLACEMENT THERAPY



Oral Co-Administration

NEXT-GENERATION ERT's

Chaperone Co-Formulation

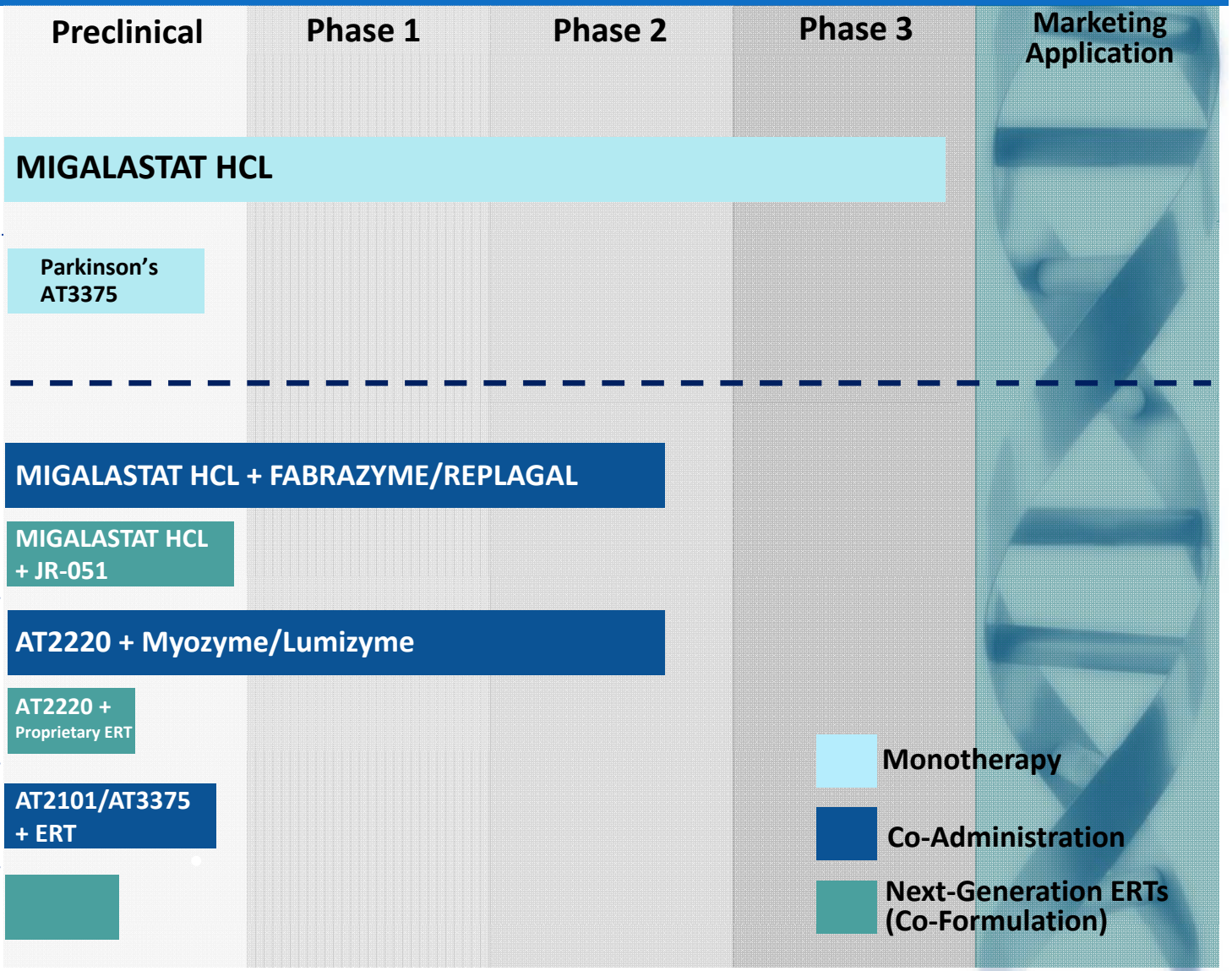
Chaperone-Advanced Replacement Therapy

CO-ADMINISTRATION
(ORAL CHAPERONES + MARKETED ERTs)

NEXT-GENERATION ERTs
(IV CO-FORMULATED CHAPERONES + PROPRIETARY ENZYMES)

NEXT-GENERATION ERTs WITH IMPROVED DELIVERY REGIMEN

Advanced Product Pipeline

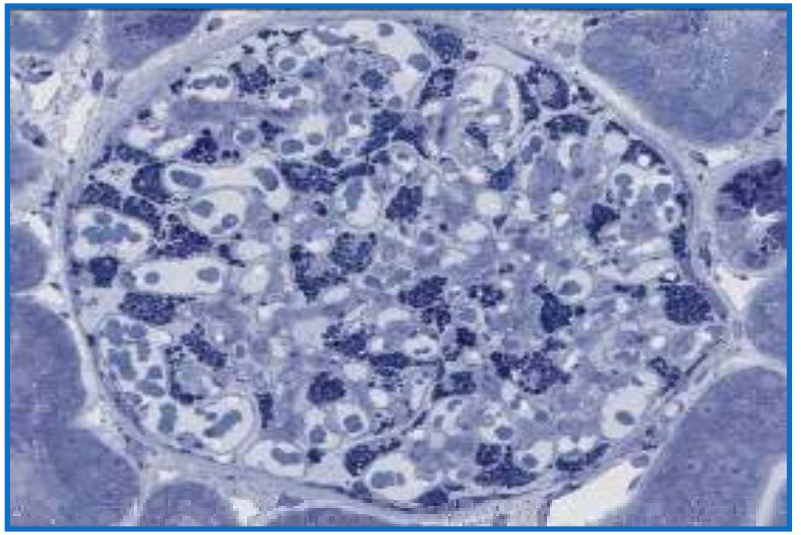


PHARMACOLOGICAL CHAPERONES

MONOTHERAPY DEVELOPMENT IN FABRY DISEASE

Fabry Disease Overview

- **Fatal, progressive, multi-system lysosomal storage disease**
- **Inherited GLA mutations**
- **X-linked**
- **Renal failure, cardiac failure, stroke**
- **5-10K diagnosed WW (51% female/49% male*)**
- **FY12 ERT sales of $873M WW**
  - $195M US (Fabrazyme conditional approval)
  - $678M ex-US (Fabrazyme and Replagal full approval)
  - Presence of antibodies [against α-Gal A] may reflect worse treatment outcome[1]



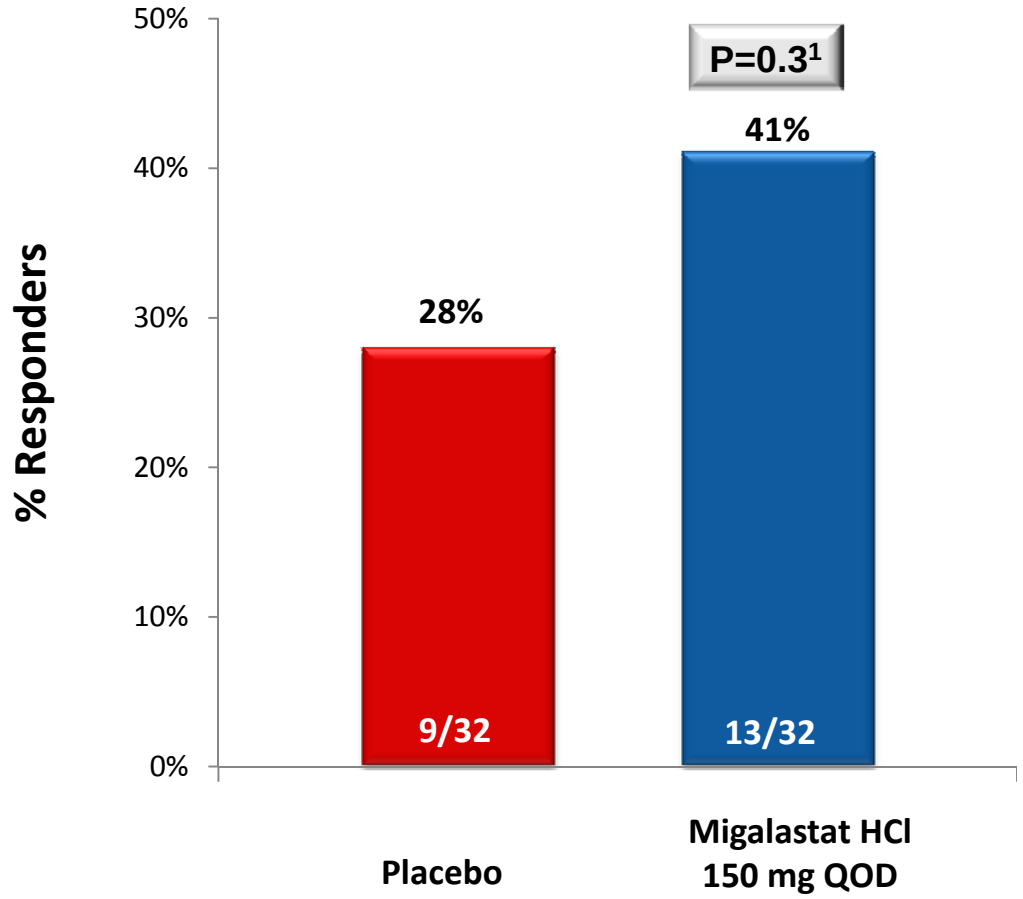
Kidney GL-3

*Fabry Registry 2011 [1]Rombach *et al.*, **PLoS ONE,** 2012 Oct

Migalastat HCl* Monotherapy for Fabry Disease

Phase 3 Study 011: Top-Line 6-Month (Stage 1) Results

Primary Endpoint at Month 6 – Responder Analysis (ITT)
Response: ≥ 50% Reduction from Baseline in Kidney Interstitial Capillary GL-3



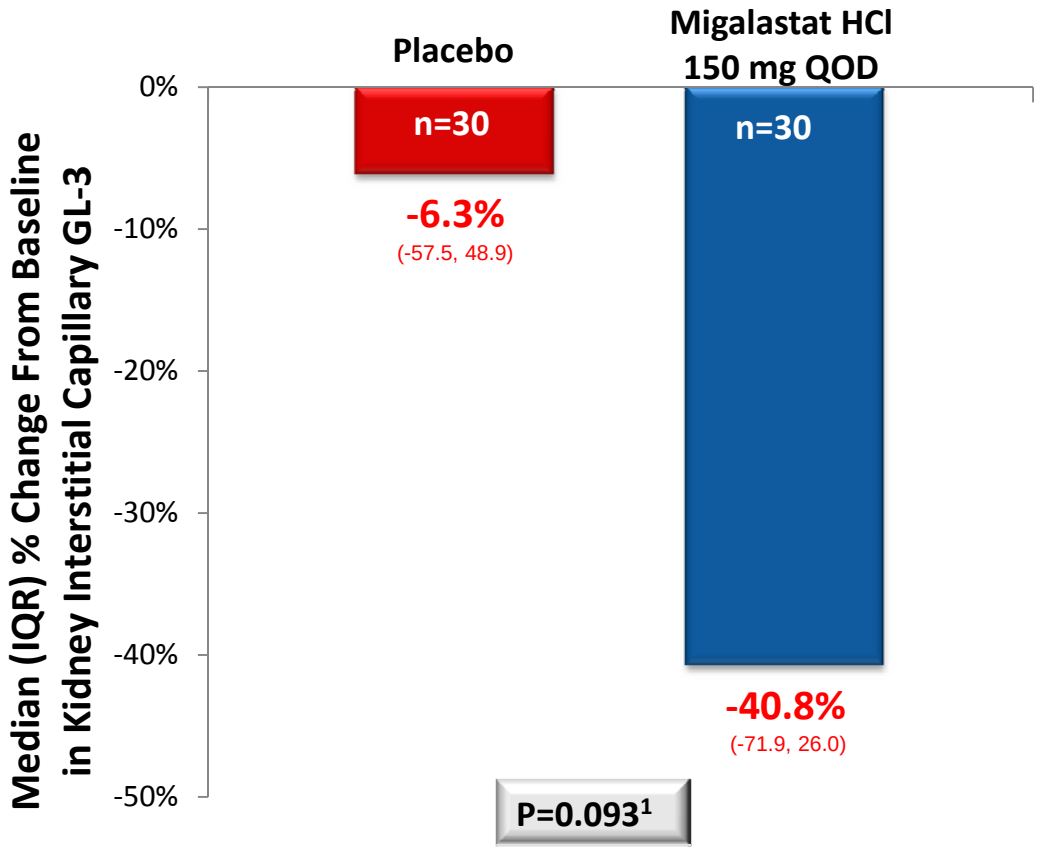
* migalastat is not authorized for use and is an investigational product

[1] Difference=12.5% (95% CI: -13.4, 37.3). Migalastat HCl minus placebo in % responders. P-value based on exact Cochran-Mantel-Haenszel test stratified by gender. Subjects with baseline biopsy but missing month 6 biopsy counted as a failure.

Migalastat HCl Monotherapy for Fabry Disease

Phase 3 Study 011: Top-Line 6-Month (Stage 1) Results

Secondary Analysis of Primary Endpoint at Month 6 (mITT*)
Median Percent Change From Baseline



*mITT: Subjects who had a baseline and at least one on-therapy assessment. Median baseline average number of inclusions per capillary (0.23 placebo, 0.18 Migalastat HCl)
[1]p-value from ANCOVA based on ranked observations adjusting for baseline and sex

Migalastat HCl Monotherapy for Fabry Disease

Phase 3 Study 011: 6-Month (Stage 1) Safety

Most Common Treatment Emergent Adverse Events (≥ 10% of Subjects)		
Adverse event	Placebo (n=33)	Migalastat HCl (n=34)
Any Event	91%	91%
Headache	21%	35%
Fatigue	12%	12%
Nausea	12%	9%
Nasopharyngitis	15%	6%
Paresthesia	9%	12%

No Serious Adverse Events Deemed by Investigators to be Treatment-Related

No Withdrawals Due to Adverse Events

Migalastat HCl Monotherapy for Fabry Disease

Study 011 Status and Upcoming Milestones

1H13 | **2H13**

Study 011 12-Month Treatment Extension

Long-Term Open-Label Extension Study*

Stage 2 (12-month) data

- Pre-specified descriptive comparisons
- 12-month data from migalastat HCl group
- 6-month data from placebo crossover group

Mid-2013 FDA Meeting Anticipated

- 6-month analysis is Stage 1 data
- FDA to consider entirety of Study 011 (Stage 1+2) data for NDA submission
- No single endpoint will be determinative

*Patients rolled over following 12-month treatment extension

Migalastat HCl Monotherapy for Fabry Disease

Phase 3 Study 012: Overview and Status

Ongoing 18-Month Open-Label Study Comparing Migalastat HCl (150 mg QOD) to ERT (Fabrazyme and Replagal) in Fabry Patients with Amenable Mutations*

- Switch to migalastat HCl or remain on ERT
- 60 total patients (1.5:1 randomization)
- No kidney biopsies
- Clinical outcome is renal function (Iohexol GFR)
- Data anticipated 2H14

*GLA mutations identified as amenable to migalstat HCl in a cell-based assay

CHAPERONE-ERT COMBINATION PLATFORM

FOR LYSOSOMAL STORAGE DISEASES

CHAPERONE-ADVANCED REPLACEMENT THERAPY

LSD Products Today

Potential Limitations

Enzyme Instability in Blood & Infusion Bag

Dosing Limitations & Duration of Infusion

Poor Enzyme Uptake into Tissues

Immunogenicity

Chaperone-Advanced Replacement Therapy™

CHART Offers Multiple Potential Ways to Improve ERT Outcomes for Patients

CHART™
CHAPERONE-ADVANCED REPLACEMENT THERAPY

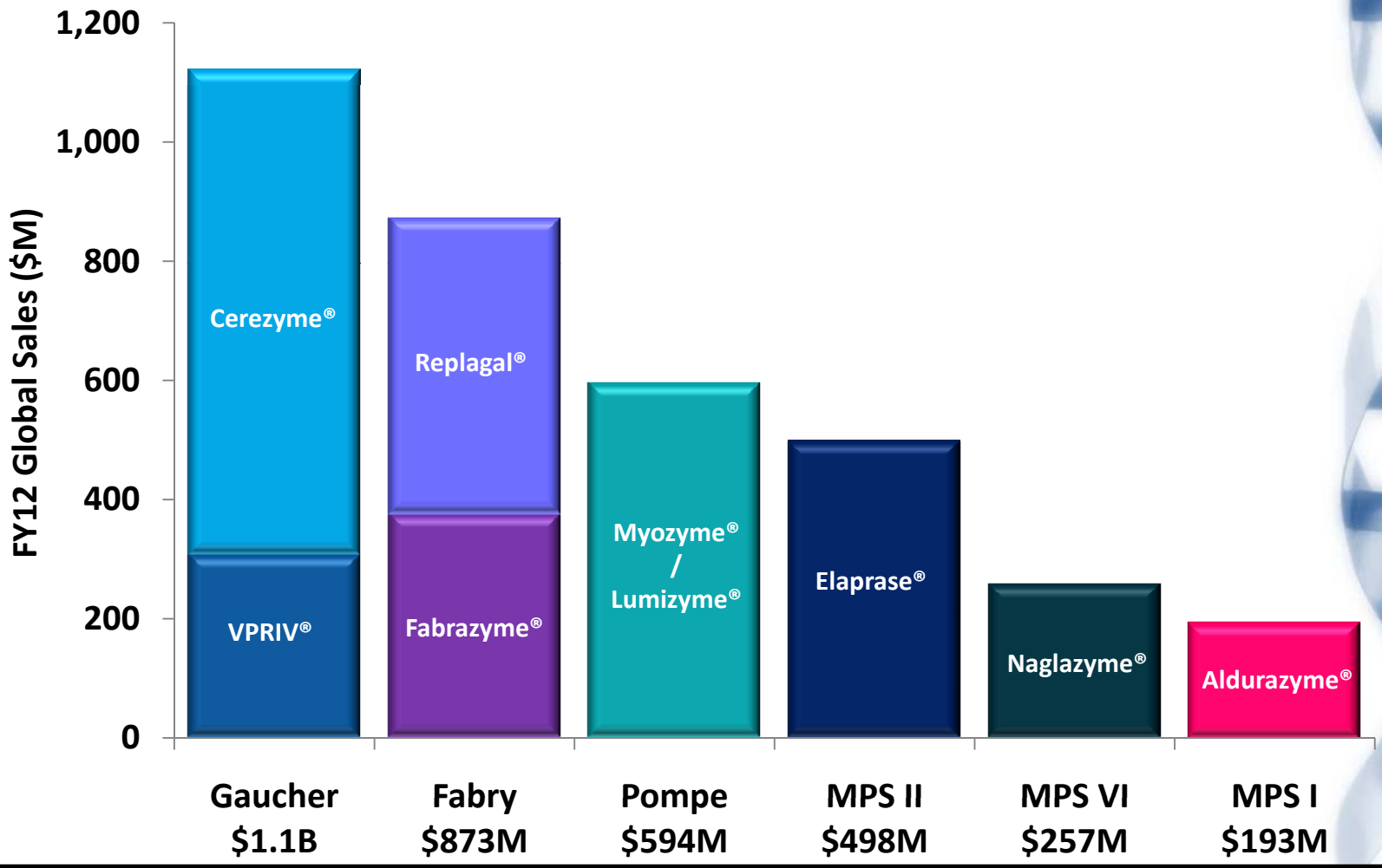
Proposed MOA: bind to and stabilize enzyme, keeping properly folded

- Increase active enzyme in circulation
- Increase enzyme uptake into tissues
- Mitigate immune response
- Improve dosing/ delivery

*Potential benefits under investigation in clinical and preclinical studies

$3.5B Current ERT Market for LSDs

Currently Approved ERTs Generated $3.5B in FY12 Global Sales*
>15 ERTs in Development Today



*Source: 10-Ks from Shire, Sanofi, and BioMarin. Sales of Elelyso for Gaucher disease not shown.

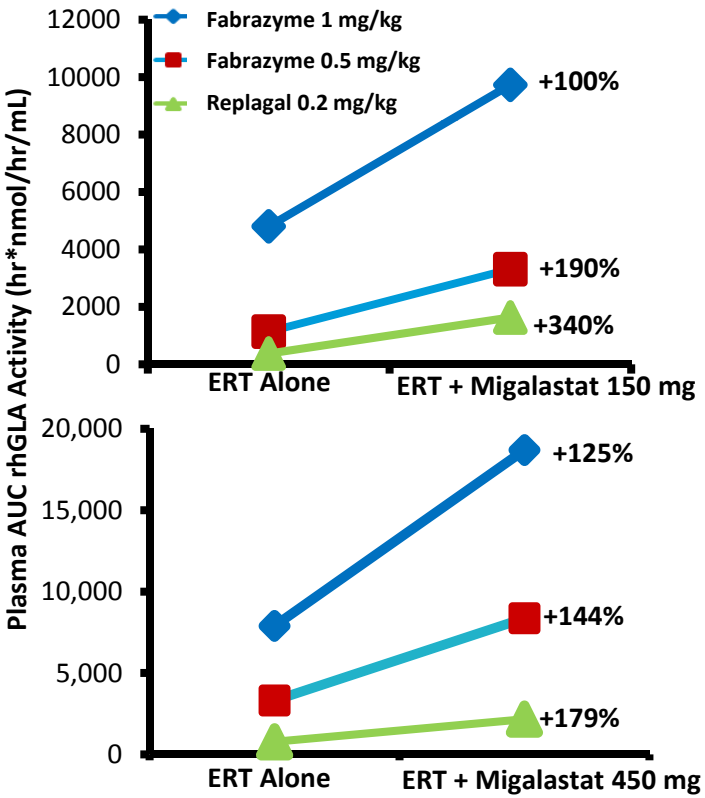
CHAPERONE-ERT COMBINATIONS FOR FABRY DISEASE

Fabry Chaperone-ERT Co-Administration

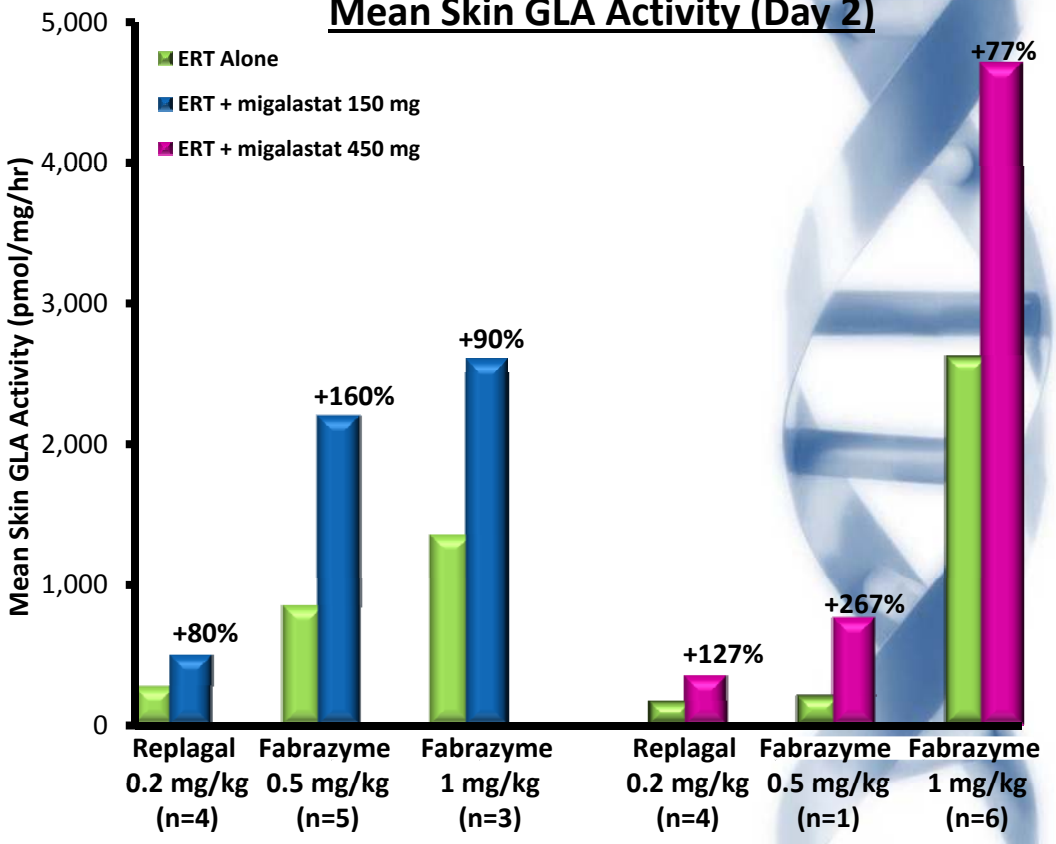
Phase 2 Study 013: Plasma Enzyme Activity and Tissue Uptake[1]

Oral Migalastat HCl* Co-Administered with Fabrazyme or Replagal Led to Consistent Increases in Active Plasma Enzyme Levels and Tissue Uptake

Plasma rhGLA Activity (Area Under Curve)



Mean Skin GLA Activity (Day 2)



[1]Bichet, *et al.,* A Phase 2a Study to Investigate the Effect of a Single Dose of Migalastat HCl, a Pharmacological Chaperone, on Agalsidase Activity in Subjects with Fabry Disease, **LDN WORLD 2013**

*Single oral dose 2 hours prior to ERT infusion

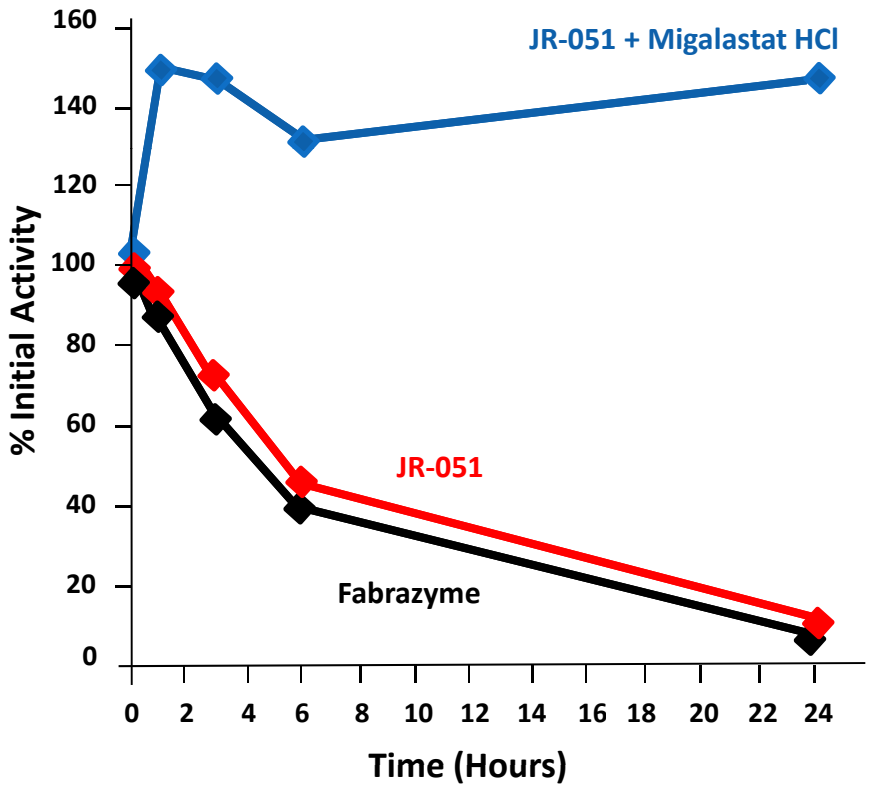
Fabry Chaperone-ERT Co-Formulation

Proprietary ERT JR-051 + Migalastat HCl*

Preliminary Results

Stabilization of JR-051 *ex vivo*

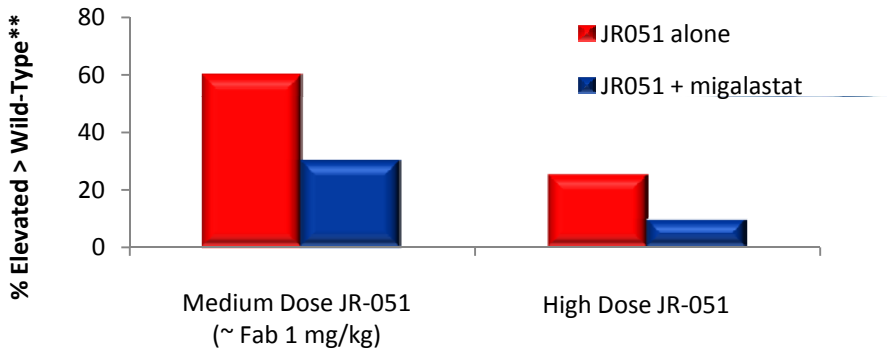
Migalastat HCl Prevents Loss of Enzyme Activity in Blood



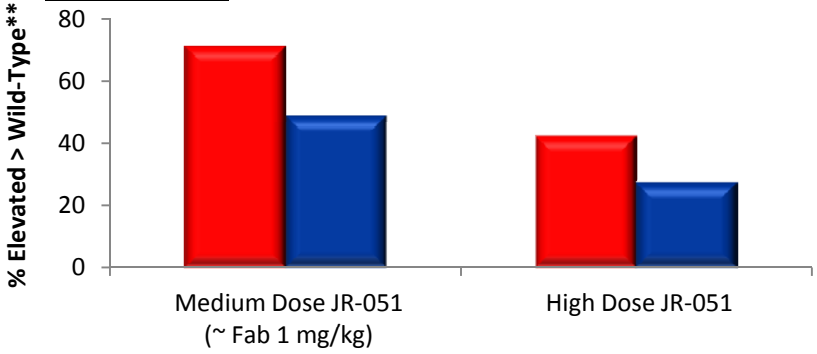
JR-051 +/- Migalastat HCl in GLA Knock-Out Mice (Repeat-Dose IV Administration)

Co-Formulation Results in Significantly Greater GL-3 Reduction than Previously Observed

Heart GL-3



Kidney GL-3



*JR-051 designed to be biosimilar to Fabrazyme
**0 = wild-type, 100 = untreated KO mouse

Fabry Chaperone-ERT Co-Formulation

Development Status and Anticipated Milestones

Advancing JR-051 + Migalastat HCl Toward Clinic

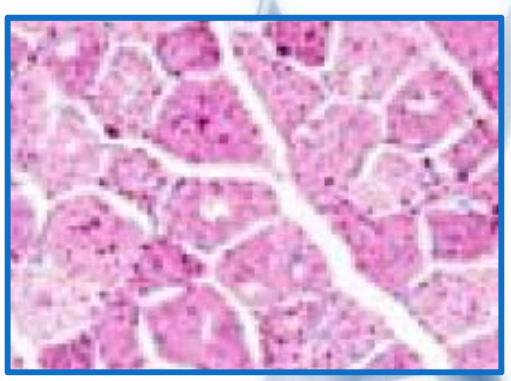
- Now manufacturing at 2,000 L scale
- IND-enabling studies underway
- Potential to enter clinic 4Q13/1Q14

CHART PROGRAMS FOR POMPE DISEASE

CHAPERONE-ADVANCED REPLACEMENT THERAPY

Pompe Disease Overview

- **Severe, fatal neuromuscular disease**
- **Inherited deficiency in lysosomal enzyme GAA**
- **Glycogen accumulation**
- **First and only approved ERTs (recombinant GAA): Myozyme/Lumizyme ($594M in FY12 sales)**
  - Standard infusion every-other-week
  - Infusion-associated reactions in ~50% of late-onset patients[1]
  - Attenuated therapeutic response in infantile Pompe patients with high sustained antibody titer[2]
  - High antibody titer shown to affect treatment in adults[3]



ELEVATED GLYCOGEN IN MUSCLE

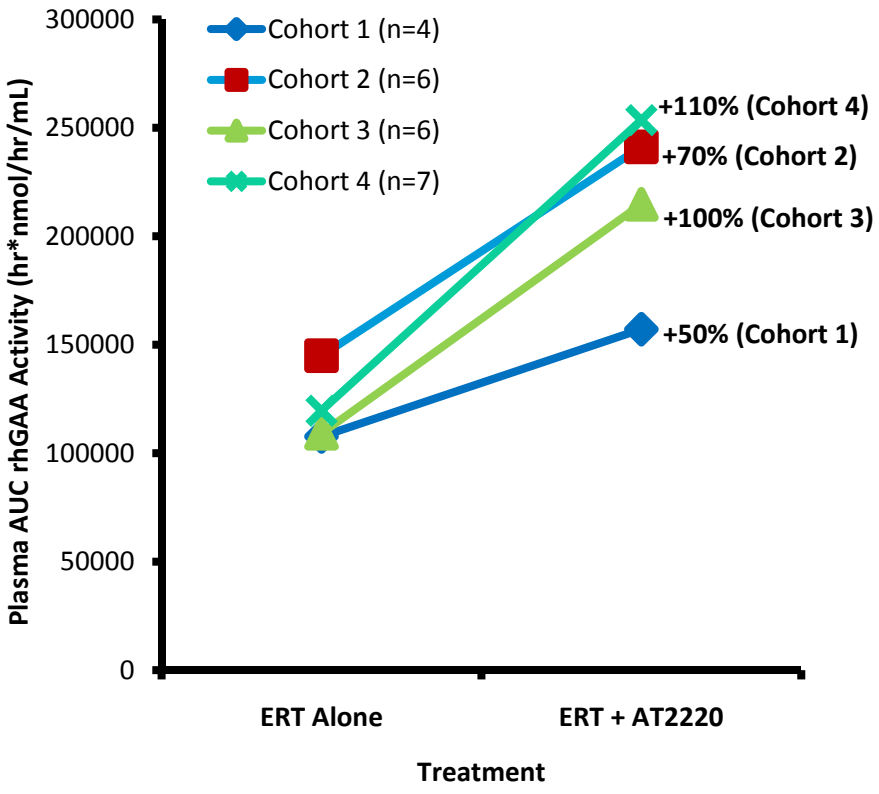
[1]Banati *et al.,* **Muscle Nerve**, 2011 Dec. ; [2]Banugaria *et al.*, **Gen. Med.,** 2011 Aug.; [3]de Vries *et al.,* **Mol Genet Metab**., 2010 Dec.

Pompe Chaperone-ERT Co-Administration

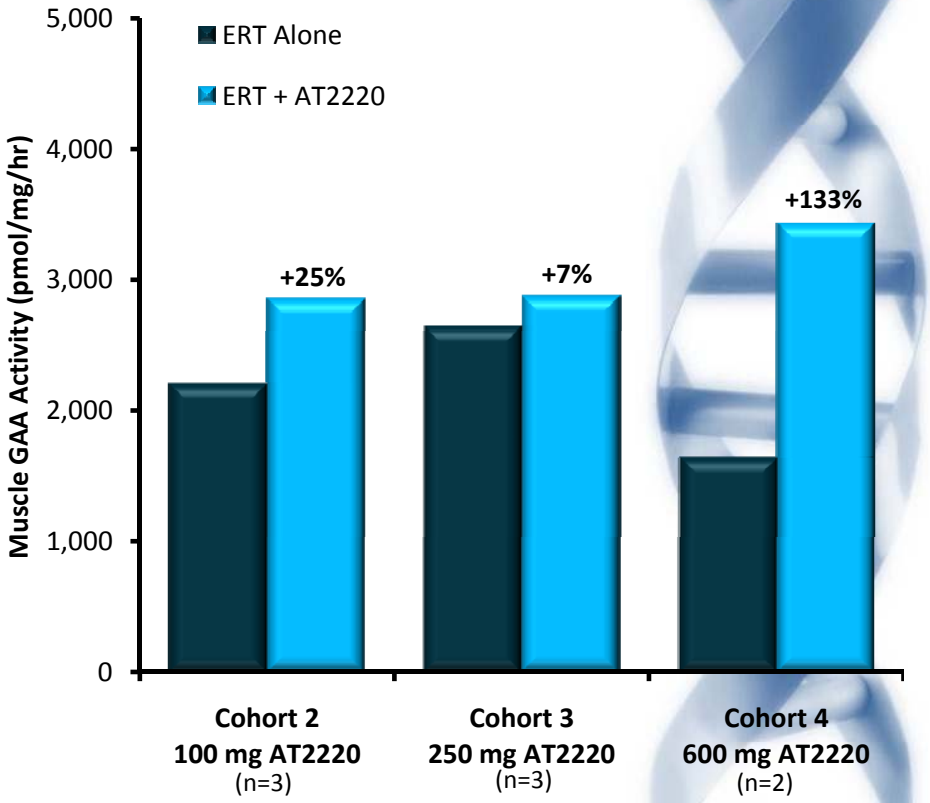
Phase 2 Study 010: Plasma Enzyme Activity and Tissue Uptake[1]

Oral AT2220 Co-Administered with Myozyme/Lumizyme Also Leads to Consistent Increases in Plasma Enzyme Activity and Tissue Uptake

Plasma AUC rhGAA Activity



Muscle GAA Activity (Day 3)*



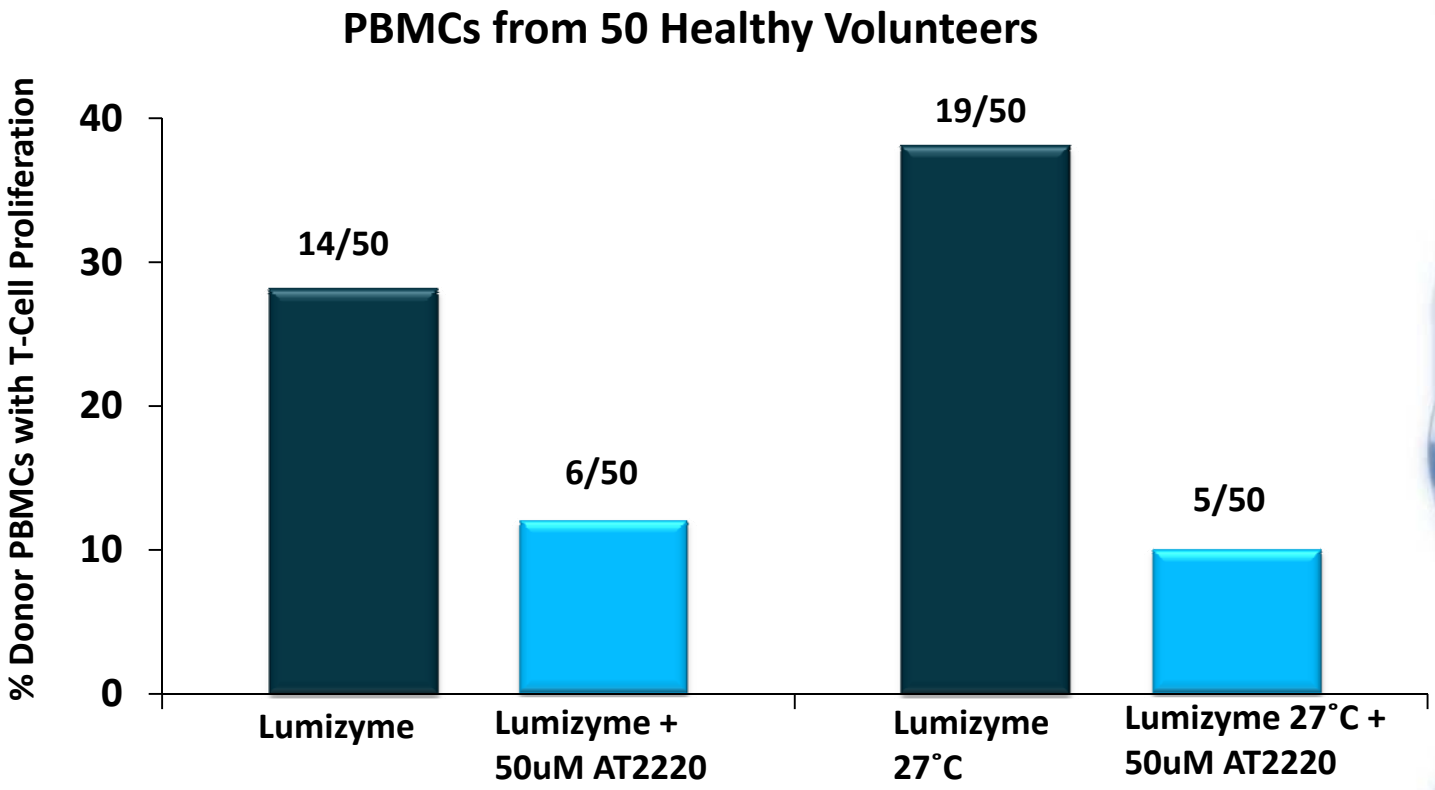
[1]Kishnani, *et al.,* A Phase 2a Study to Investigate Drug-Drug Interactions between Escalating Doses of AT2220 (Duvoglustat Hydrochloride) and Acid Alfa-Glucosidase in Subjects with Pompe Disease, **LDN WORLD 2013**

*Cohort 1 (AT2220 50 mg) muscle GAA activity not shown; 50 mg dose did not demonstrate meaningful change in tissue uptake (muscle)

Pompe Chaperone-ERT Co-Administration

Potential to Mitigate ERT Immunogenicity

AT2220 Mitigates Human T-Cell Response Induced by Lumizyme *ex vivo* and May Significantly Reduce Immunogenicity of Lumizyme

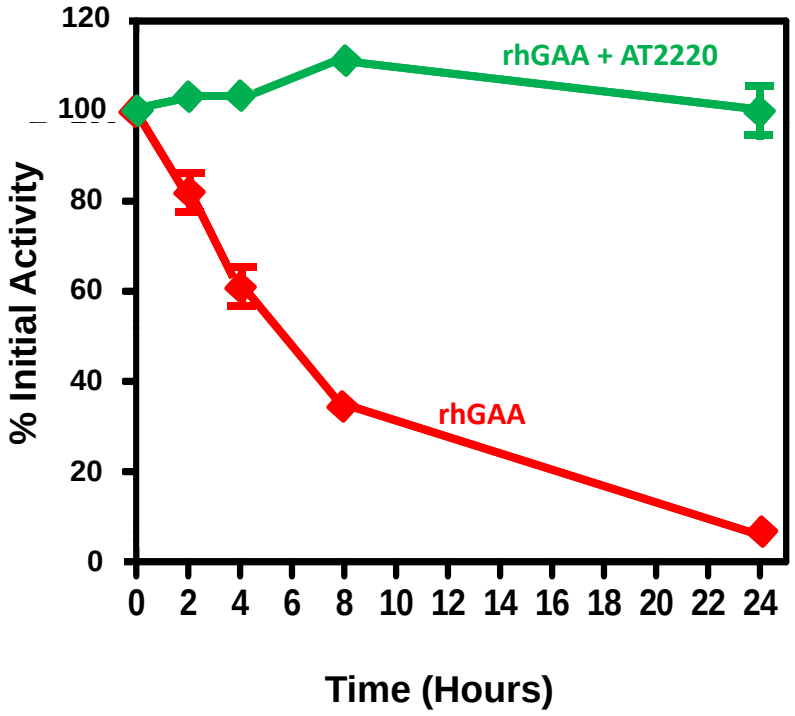


Pompe Chaperone-ERT Co-Formulation

AT2220 + Myozyme/Lumizyme (rhGAA Enzyme)[1]

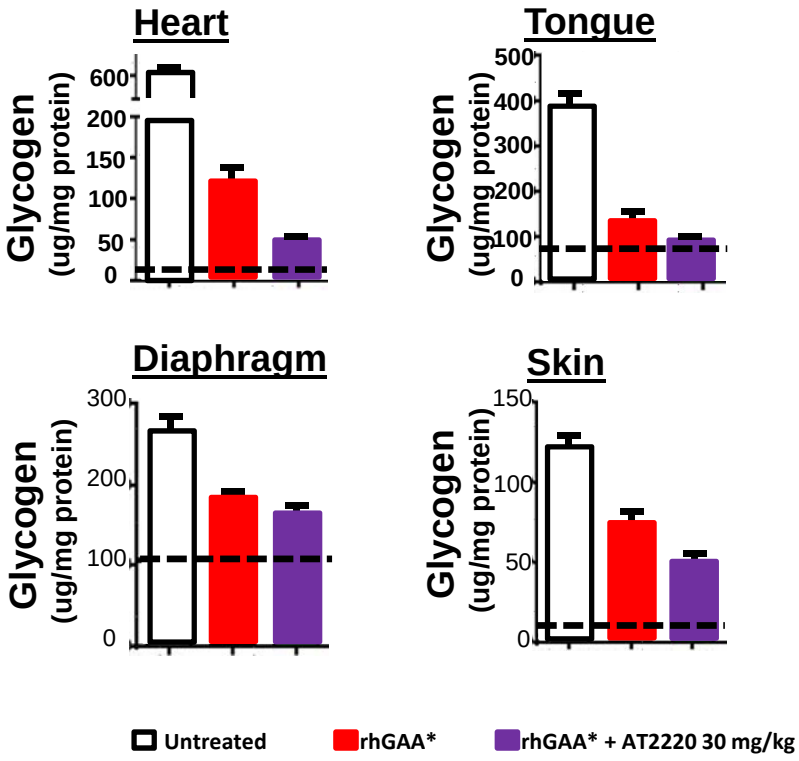
Stabilization of rhGAA *ex vivo*

AT2220 Prevents Loss of Enzyme Activity in Blood



rhGAA +/- AT2220 in GAA Knock-Out Mice (Repeat-Dose IV Administration)

Co-Formulation Results in Significantly Greater Glycogen Reduction

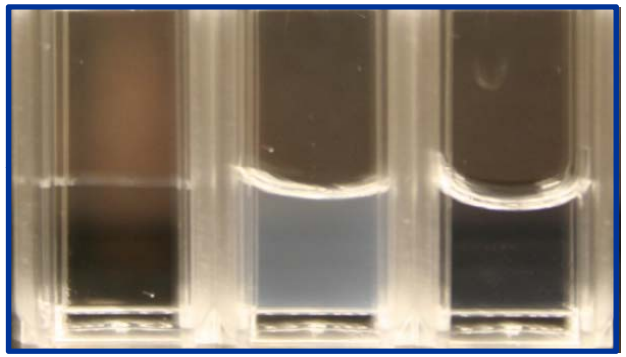


[1]Khanna, *et al.,* Exploring the Use of a Co-formulated Pharmacological Chaperone AT2220 with Recombinant Human Acid Alpha-Glucosidase for Pompe Disease, **LDN WORLD 2013**

Pompe Chaperone-ERT Co-Formulation

Next-Generation ERT: SubQ Delivery Potential

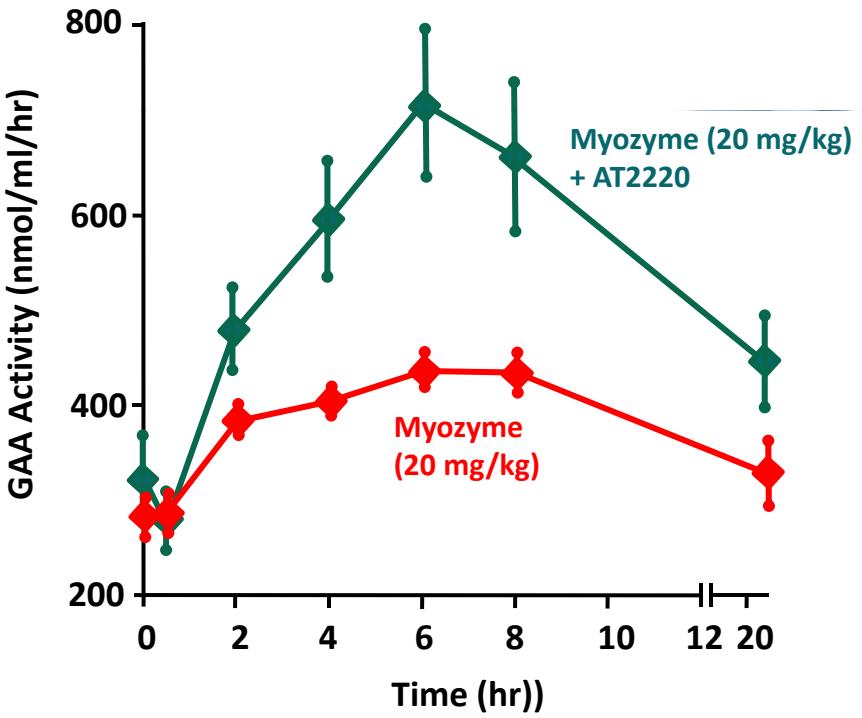
Increased ERT Stability and Prevention of Aggregation



Myozyme	-	+	+
AT2220	-	-	+

- Aggregation assessed after 4 weeks at 37˚C

Increased Circulating Levels of Active rhGAA in Rats

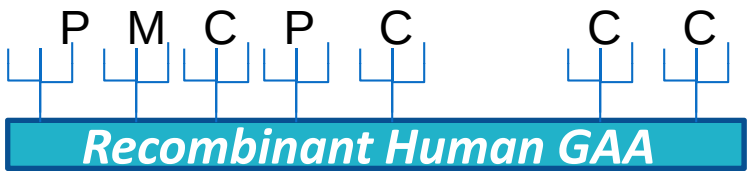


Pompe Chaperone-ERT Co-Formulation

Next-Generation ERT (AT2220 + Proprietary Enzyme)

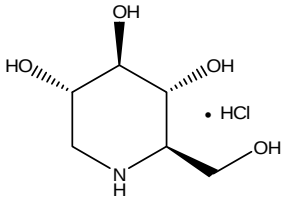
Combining Core Pharmacological Chaperone Technology with Advanced Biologics Capabilities to Create a Next-Generation Pompe ERT

Proprietary Recombinant Human GAA Enzyme



+

AT2220 Small Molecule Stabilizer



- Increased exposure & tissue uptake
- Reduced immunogenicity
- Formulation for SQ route of administration

LAUREATE BIOPHARMA

Next-Generation ERT

Potential Improvements

- Optimized glycosylation (e.g., M6-P)
- De-immunization

CHART Pathways for Pompe Disease

Amicus Therapeutics

Co-Administration (AT2220-IV + Marketed ERTs) → **Repeat-dose clinical study expected to begin 3Q13**

Next-Generation ERT (AT2220 + Proprietary rhGAA Enzyme) → **Preclinical studies underway**

2013 Anticipated Milestones

Building Shareholder Value

Migalastat HCl Monotherapy for Fabry Disease

✓ Study 011 6-Month data (Stage 1) at LDN WORLD	Feb. 2013
▪ Top-line Study 011 12-month data (Stage 2)	2Q13
▪ FDA meeting to discuss U.S. approval pathway	Mid-2013

Pompe Chaperone-ERT Co-Administration

✓ Phase 2 Study 010 data at LDN WORLD (all 4 cohorts)	Feb. 2013
▪ Initiation of repeat-dose clinical study	3Q13

Fabry Chaperone-ERT Co-Administration

✓ Phase 2 Study 013 data at LDN WORLD (oral migalastat HCl 450 mg + ERT)	Feb. 2013

Fabry Chaperone-ERT Co-Formulation (Migalastat HCl + JR-051)

▪ IND-enabling studies and clinical supply manufacturing	Ongoing
▪ Potential entry into clinic	4Q13/1Q14