Amicus Therapeutics

31st Annual J.P.Morgan Healthcare Conference

John F. Crowley
Chairman & CEO

At the Forefront of Therapies for Rare and Orphan Diseases™

January 9, 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

JPMorgan Healthcare Conference 2013

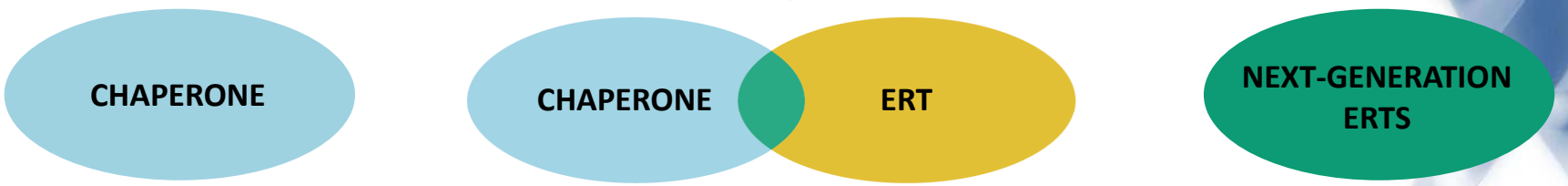
Key Messages

- Phase 3 Fabry monotherapy study (Study 011) ongoing:
  - Top-line 6-month (Stage 1) results encouraging and consistent with Phase 2 experience
  - FDA to consider “entirety of data” from both 6 and 12 months
- Pompe Chaperone-ERT co-administration repeat-dose clinical study to begin 3Q13
- Fabry Chaperone-ERT co-formulated product advancing towards clinic
- Proprietary Pompe next-generation ERT in preclinical development
- ~$100M cash at 12/31/12

Core Technology and Focus

Potential to Transform LSD Treatments

Small Molecule Pharmacological Chaperones



Oral Monotherapy

- Binds to and stabilizes patient's own natural enzyme
- Replaces need for ERT for patients with amenable genetic mutations

Oral Co-Administration

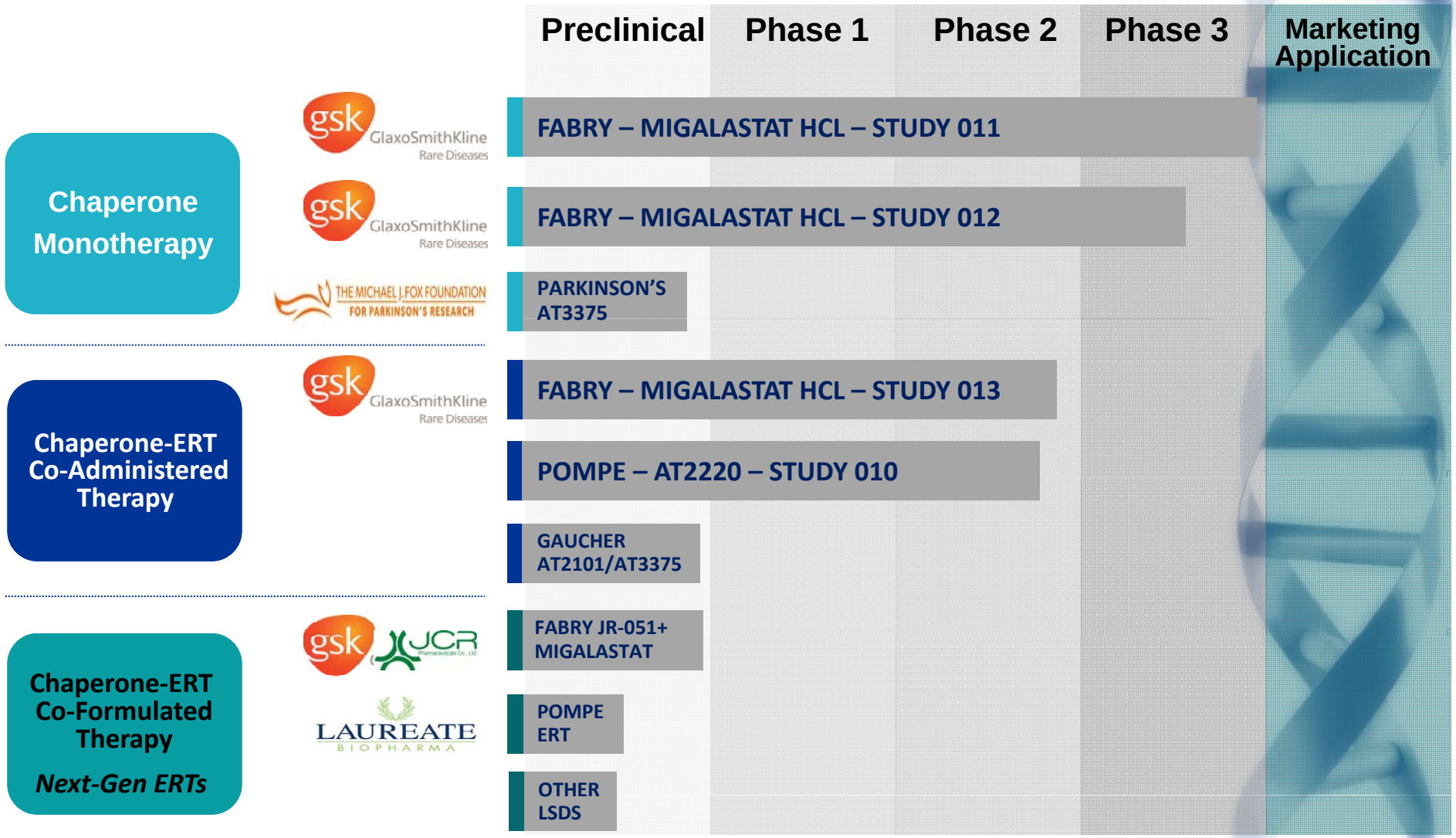
- Binds to and stabilizes currently marketed ERTs
- Increases tissue uptake
- Potentially reduces immunogenicity of ERT

Chaperone Co-Formulation

- Chaperones co-formulated with proprietary next-generation ERTs
- All benefits of co-administration…plus stability from infusion bag to target tissue

Advanced Product Pipeline

One Technology, Three Novel Applications



2013 Investment Highlights

PRODUCTS

- Migalastat HCl monotherapy: encouraging Phase 3 (Stage 1) and Phase 2 extension study results
- First-in-man Phase 2 results in Fabry and Pompe Chaperone-ERT Co-Administration

PLATFORM TECHNOLOGY

- Next-Generation ERTs in development
- Multiple potential therapeutic enhancements, including novel routes of delivery

PARTNERSHIPS

GlaxoSmithKline

JCR Pharmaceuticals Co., Ltd.

LAUREATE BIOPHARMA

FINANCIAL STRENGTH

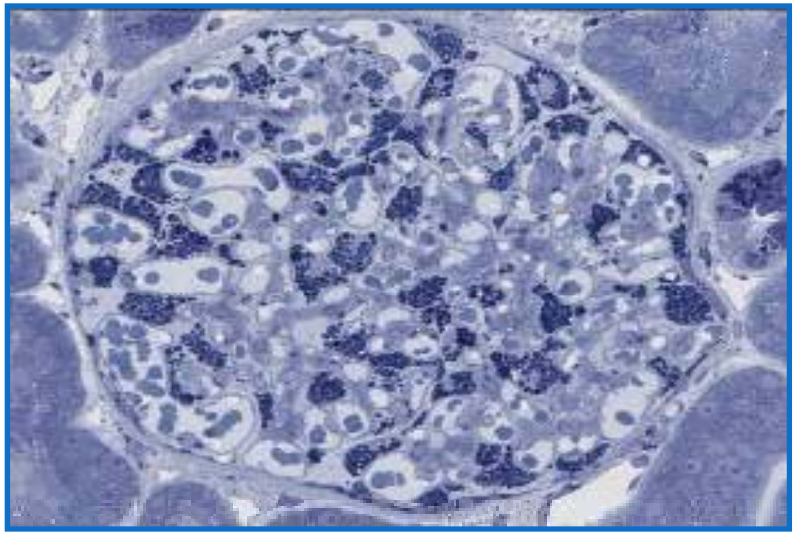
- ~$99.1M cash (12/31/12)
- GSK responsible for 60% of all Fabry development costs
- Projected cash runway 18-24 months at current spend rates
- Multiple catalysts next 12-24 months

PHARMACOLOGICAL CHAPERONES

MONOTHERAPY DEVELOPMENT IN FABRY DISEASE

Fabry Disease Overview

- Progressive, multi-system lysosomal storage disease
- Caused by inherited GLA mutations
- X-linked disease
- Mortality due to renal failure, cardiac failure, stroke
- 5 – 10K patients diagnosed WW (51% female/49% male*)
- Significantly under-diagnosed



Kidney GL-3

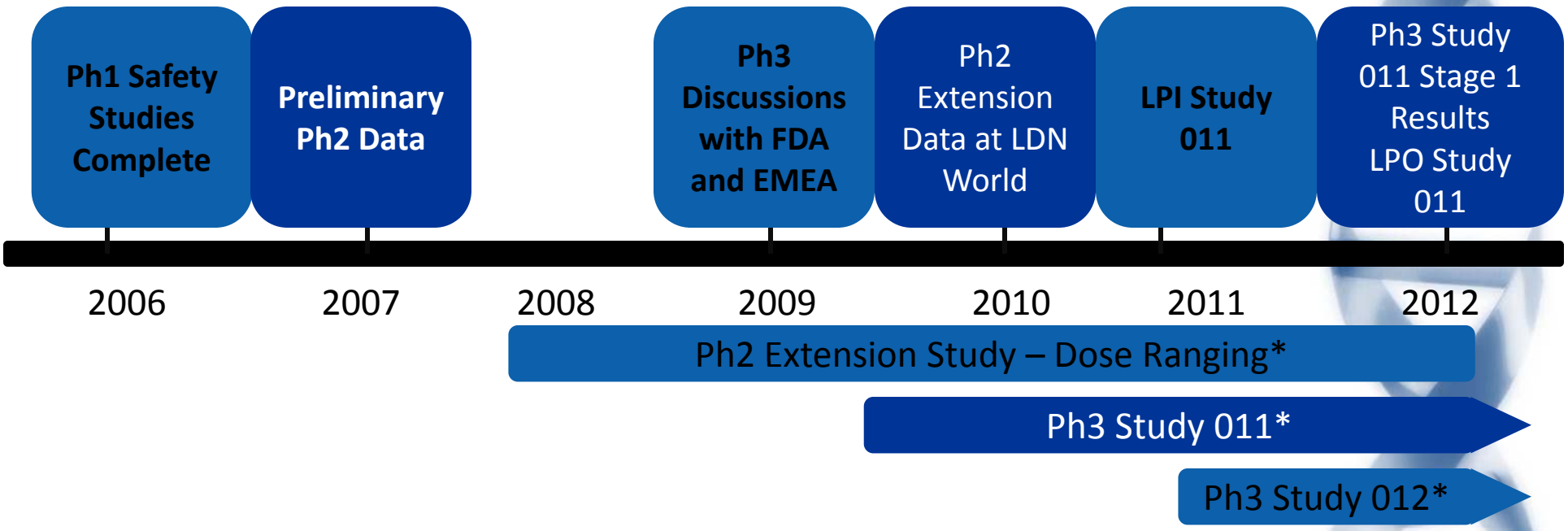
*Fabry Registry 2011

Migalastat HCl Monotherapy for Fabry Disease

Development History

January 2013 Highlights

- 102 Fabry patients WW on Migalastat HCl monotherapy as only therapy for Fabry
- >220 patient-years of data
- 57 of 59 patients completed 12 months of Study 011 and elected to continue in long-term extension studies

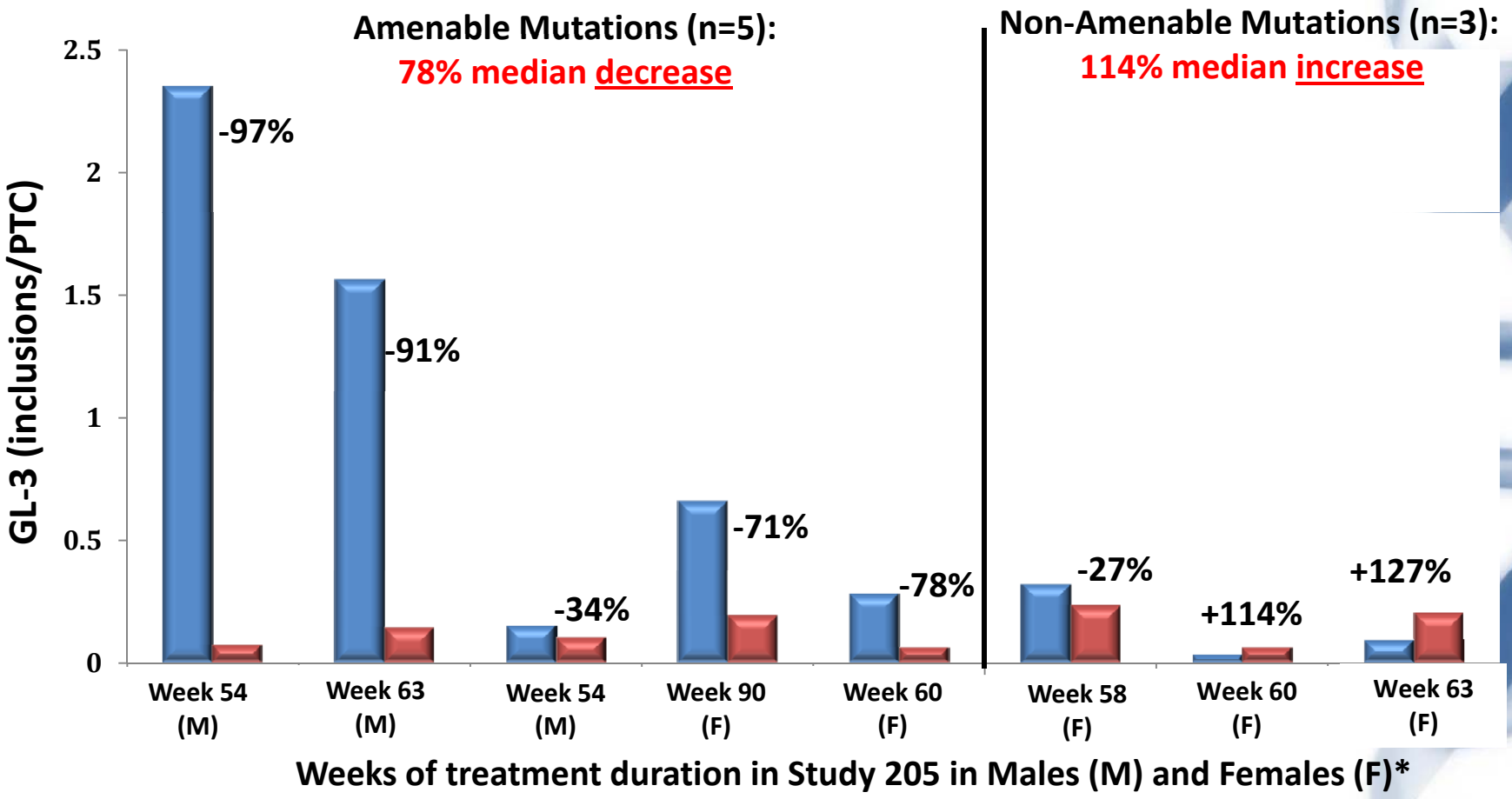


*Open-label extension studies ongoing in patients who completed Ph2 extension study and Ph3 studies

Migalastat HCl Monotherapy for Fabry Disease

Phase 2 Extension Study Update – Presented at ASN (Nov. 2012)

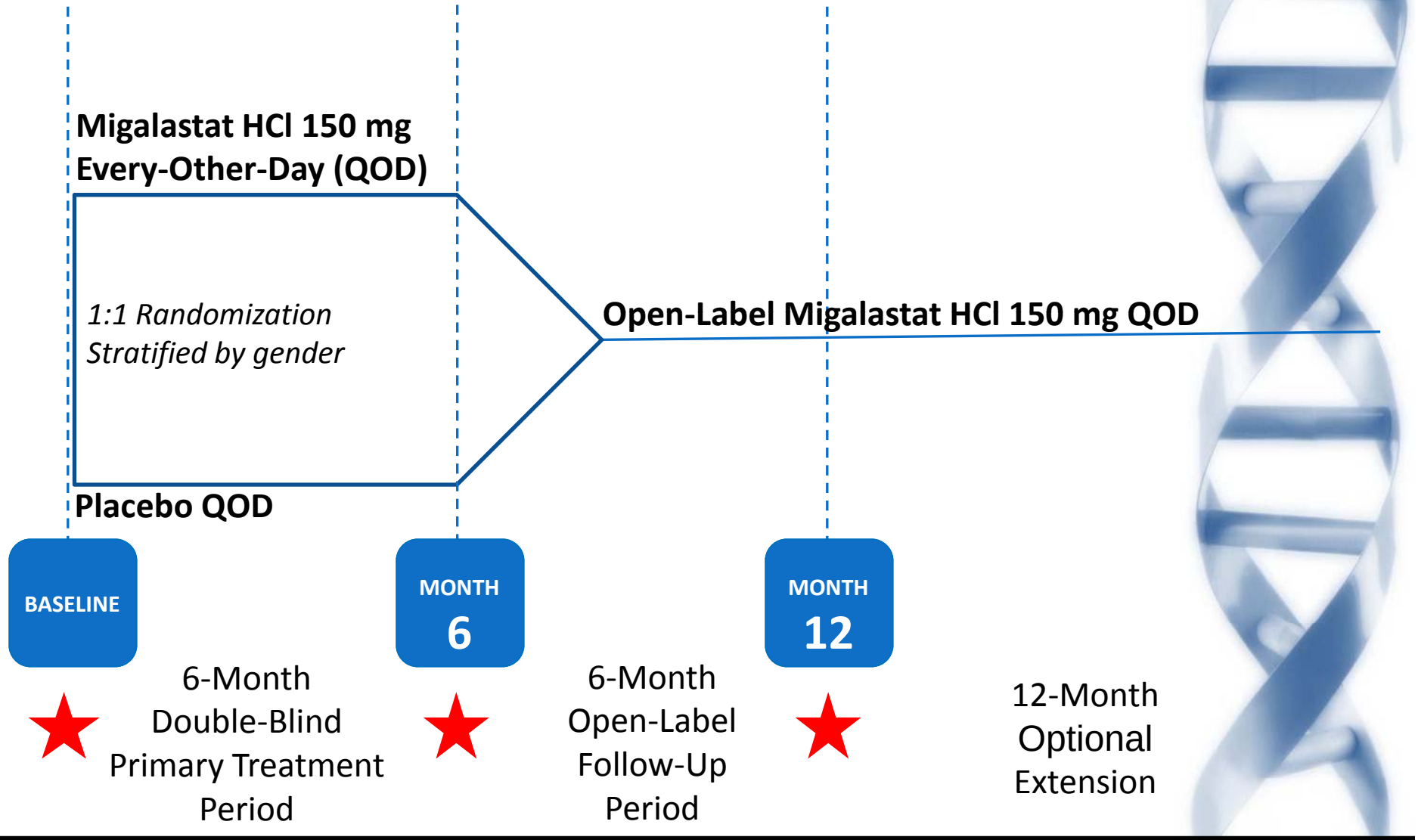
Median 78% Decrease in Kidney GL-3
Observed in Study Patients with Amenable Mutations



*All patients in Study 205 completed initial Phase 2 studies of migalastat HCl monotherapy

Migalastat HCl Monotherapy for Fabry Disease

Phase 3 Study 011: Design



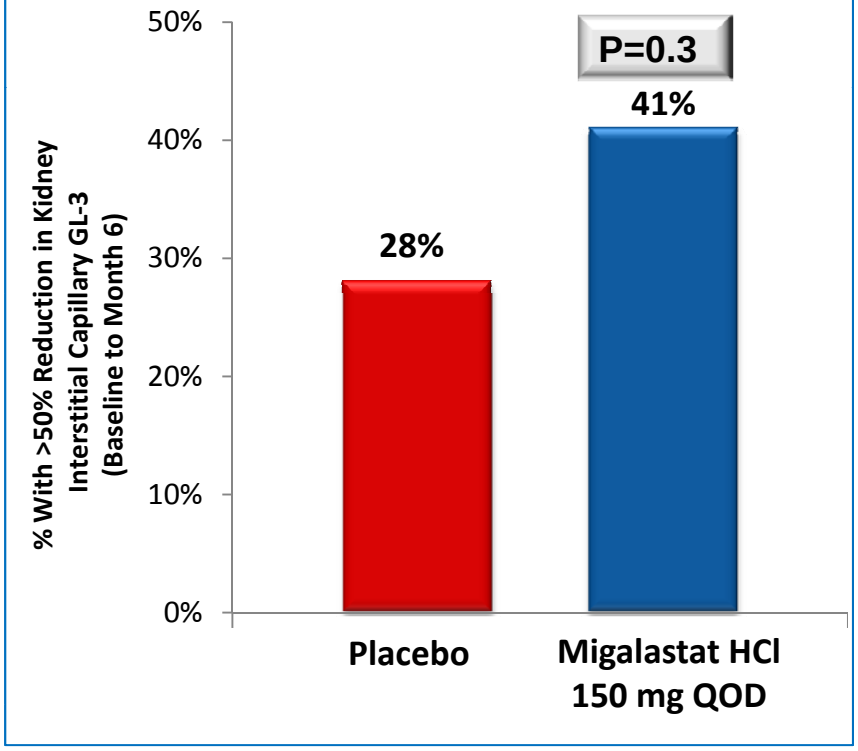
★ Kidney Biopsy

Migalastat HCl Monotherapy for Fabry Disease

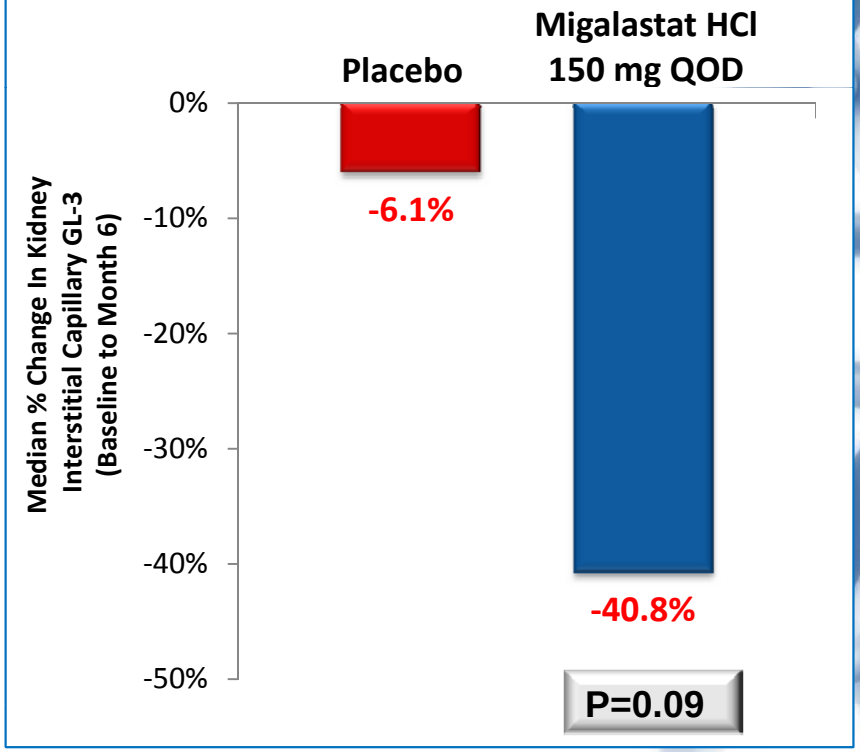
Phase 3 Study 011: Top-Line 6-Month (Stage 1) Results

Kidney Interstitial Capillary GL-3 – Surrogate Biomarker Considered Likely to Predict Clinical Benefit in Fabry Patients

6-Month Primary Endpoint Responder Analysis



6-Month Secondary Analysis of Primary Endpoint



Migalastat HCl Monotherapy for Fabry Disease

Regulatory Guidance and Path Forward

Study 011 is an Ongoing 12-Month Pivotal Study of Migalastat HCl in Patients with Fabry Disease with Amenable Mutations

U.S. FDA Feedback

- 6-month analysis is Stage 1
- FDA to consider Stage 1 and Stage 2 (12-month) data for NDA submission
- FDA will evaluate efficacy and safety based on entirety of Study 011 data (no single endpoint will be determinative)
- FDA meeting anticipated in mid-2013 to discuss US approval pathway

Migalastat HCl Monotherapy for Fabry Disease

Study 011 12-Month Analysis Plans

Pre-Specified 12-Month Descriptive Comparisons – Results Anticipated 2Q13

Study 011 Design (1:1 Randomization)		
Study Arm	**Stage 1: Month 0-6**	**Stage 2: Month 6-12***
Placebo	Placebo	SWITCH Migalastat HCl
Treatment	Migalastat HCl	Migalastat HCl

- Placebo arm Stage 2 vs. Stage 1 (migalastat HCl 6 months vs. placebo 6 months)
- Treatment arm Stage 2 vs. Stage 1 (migalastat HCl 12 months vs. 6 months)
- Treatment arm Stage 1 + placebo arm Stage 2 (pooled migalastat HCl 6 months) vs. placebo arm Stage 1
- Additional safety data

*Additional 12-24 month open-label extension following Stage 2

Migalastat HCl Monotherapy for Fabry Disease

Phase 3 Study 012: Overview and Status

- Comparing open-label oral migalastat HCl (150 mg QOD) to ERT (Replagal and Fabrazyme)
- Switch from ERT to migalastat HCl or remain on ERT (1.5:1 randomization)
- Fabry patients with amenable mutations, no kidney biopsies
- Fully enrolled with 60 patients (26 males and 34 females)
- Clinical Outcome is renal function (Iohexol GFR) at 18 months
- 18-month treatment period expected to complete in 2Q14

Migalastat HCl Monotherapy

Key Anticipated Phase 3 Inflection Points

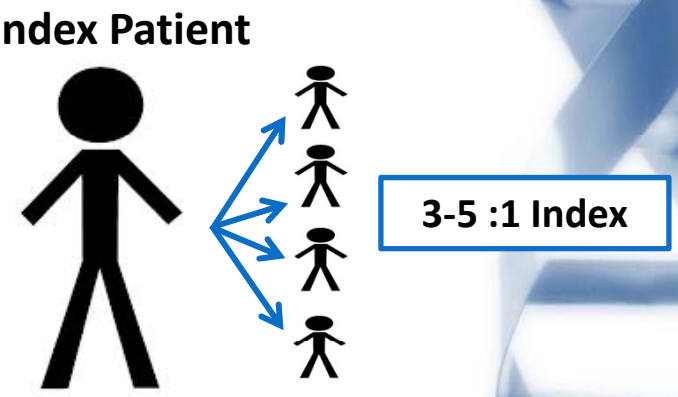
Detailed Study 011 6-month data at LDN WORLD	Feb. 2013
Study 011 12-month (Stage 2) top-line data	2Q13
FDA meeting to discuss U.S. approval pathway	Mid-2013
Completion of Study 012 18-month treatment period	2Q14
Study 012 top-line data anticipated	2H14

Migalastat HCl Monotherapy: Amenable Mutations

Evolving Epidemiology

Although ~30% of Currently Diagnosed Fabry Patients Estimated to Have Amenable Mutations, 75-100% of Patients Identified in Recent Newborn Screening Studies Have Mutations Potentially Amenable to Migalastat HCl

Recent Newborn Screening Studies	# Newborns Screened	# Confirmed Fabry Mutations	% Potentially Amenable
Burton, 2012, US	8,012	7 [1: ~1100]	TBD
Mechtler, 2011, Austria	34,736	9 [1: ~3,800]	100%
Hwu, 2009, Taiwan	171,977	75 [1: ~2300]	75%
Spada, 2006, Italy	37,104	12 [1: ~3100]	86%



Due to X-linked nature of Fabry, patients identified by screening typically yield 3-5 affected family members (Weidemann 2010)

1. Burton, **LDN WORLD Symposium,** 2012 Feb.
2. Mechtler *et al.,* **The Lancet**, 2011 Dec.
3. Hwu *et al.,* **Hum Mutation**, 2009 Jun
4. Spada *et al.,* **Am J Human Genet.**, 2006 Jul

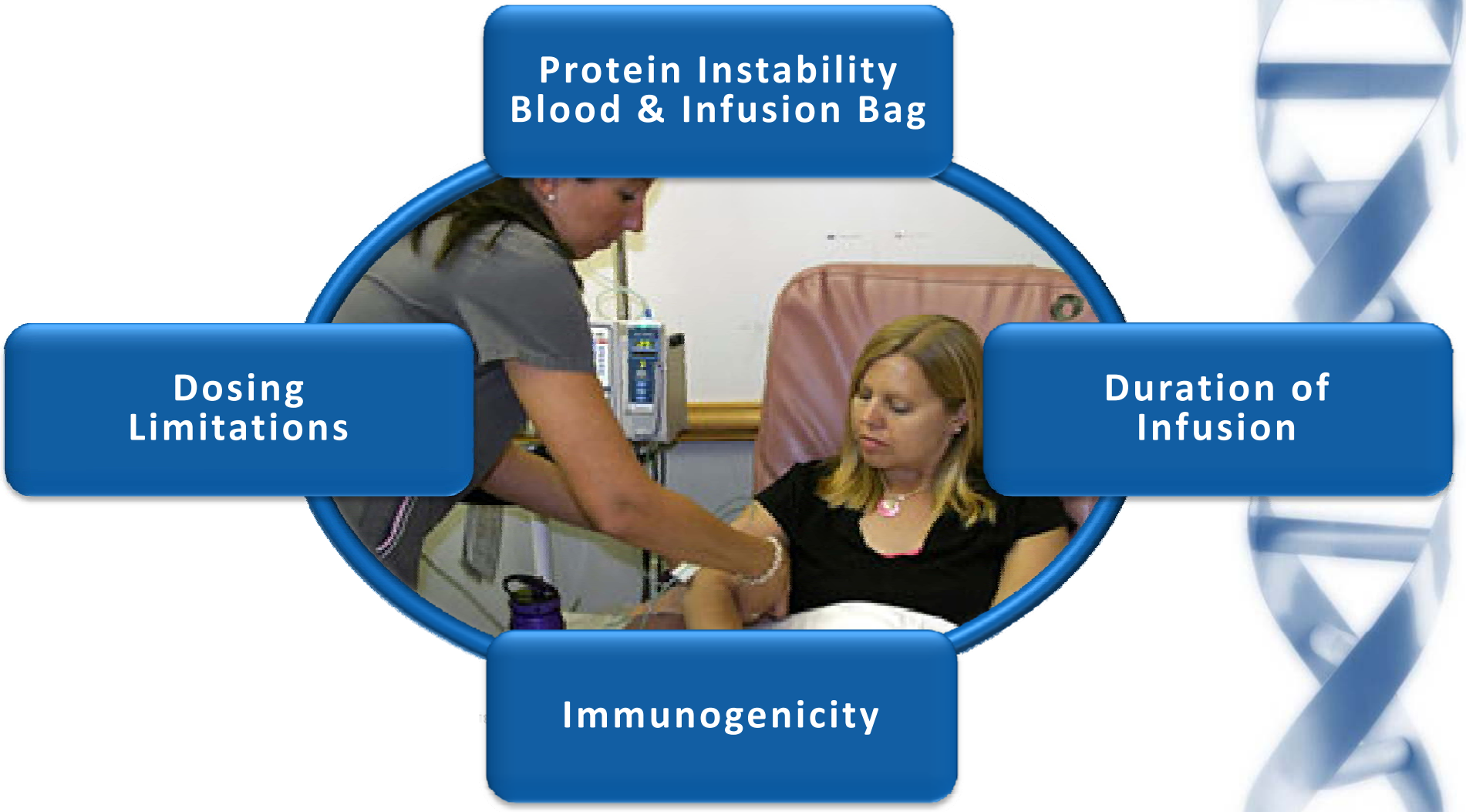
PHARMACOLOGICAL CHAPERONES

CO-ADMINISTERED WITH MARKETED ERTS

IMPROVING CURRENT ERTS FOR LYSOSOMAL STORAGE DISORDERS

LSD Products Today

Potential Issues

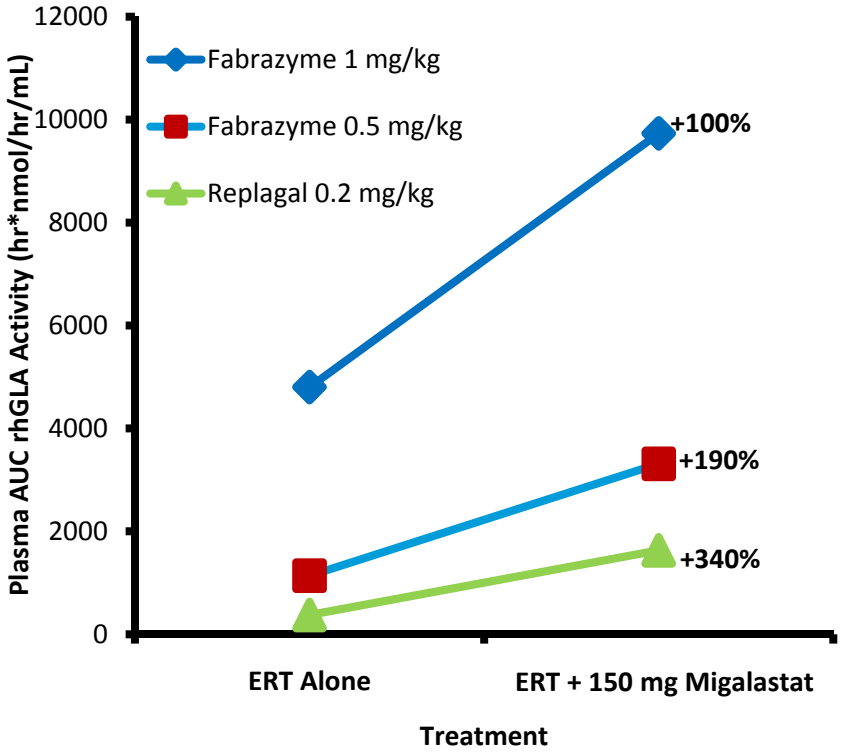


Fabry Chaperone-ERT Co-Administration

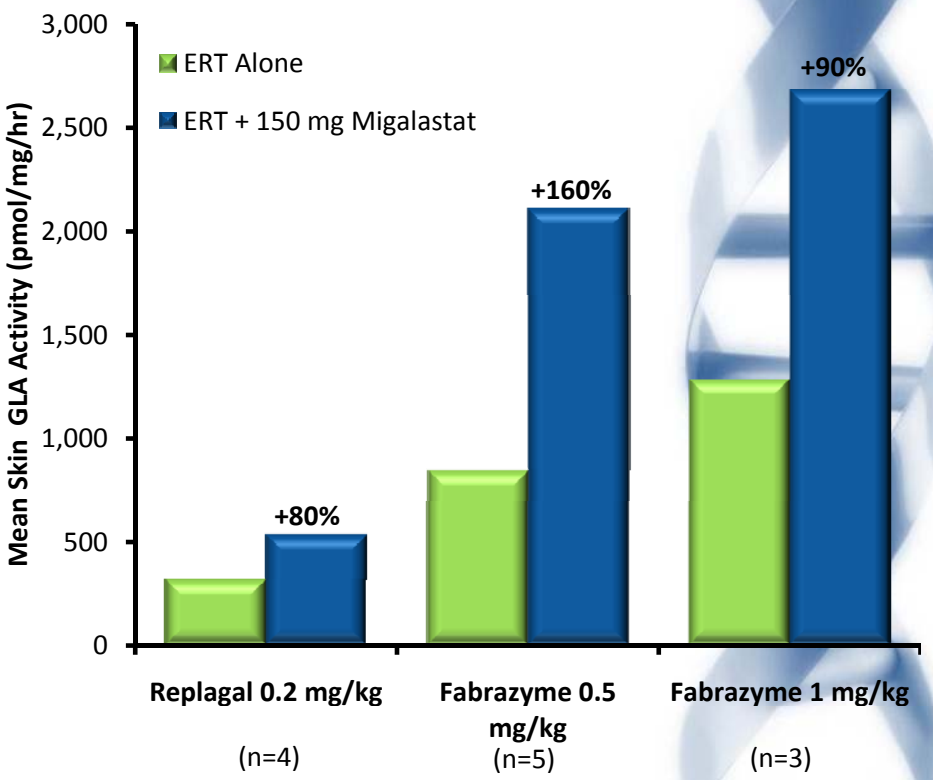
Phase 2 Study 013: Preliminary Results

Oral Migalastat HCl 150 mg* Co-Administered with Fabrazyme or Replagal Led to Consistent Increases in Levels of Active Plasma Enzyme and Tissue Uptake (Skin)

Plasma rhGLA Activity (Area Under Curve)



Mean Skin GLA Activity (Day 2)



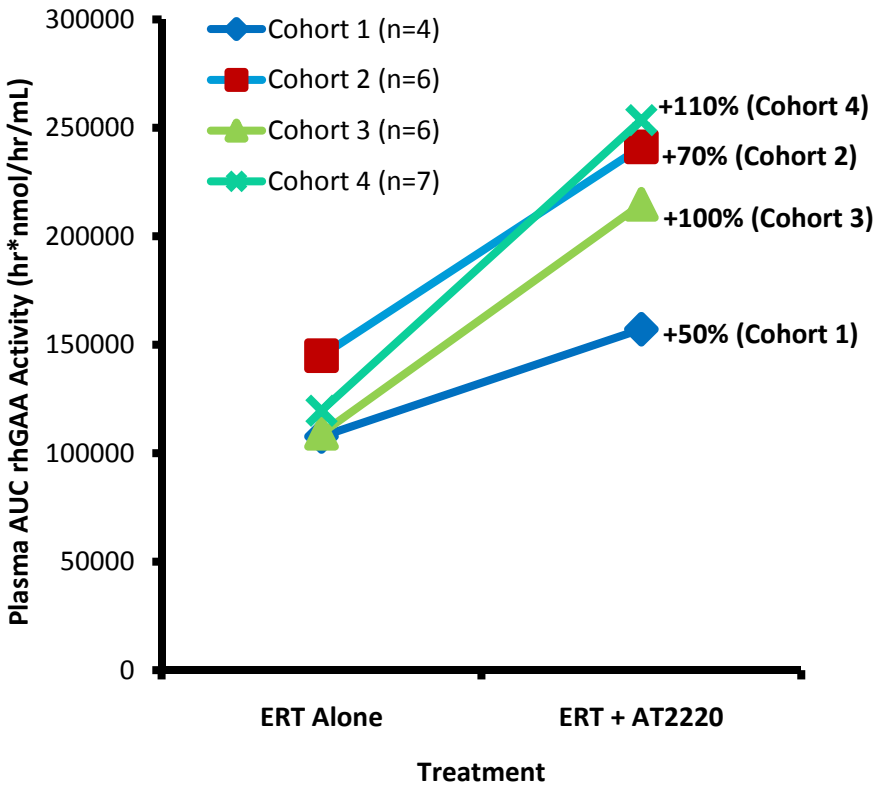
*Single oral dose 2 hours prior to ERT infusion

Pompe Chaperone-ERT Co-Administration

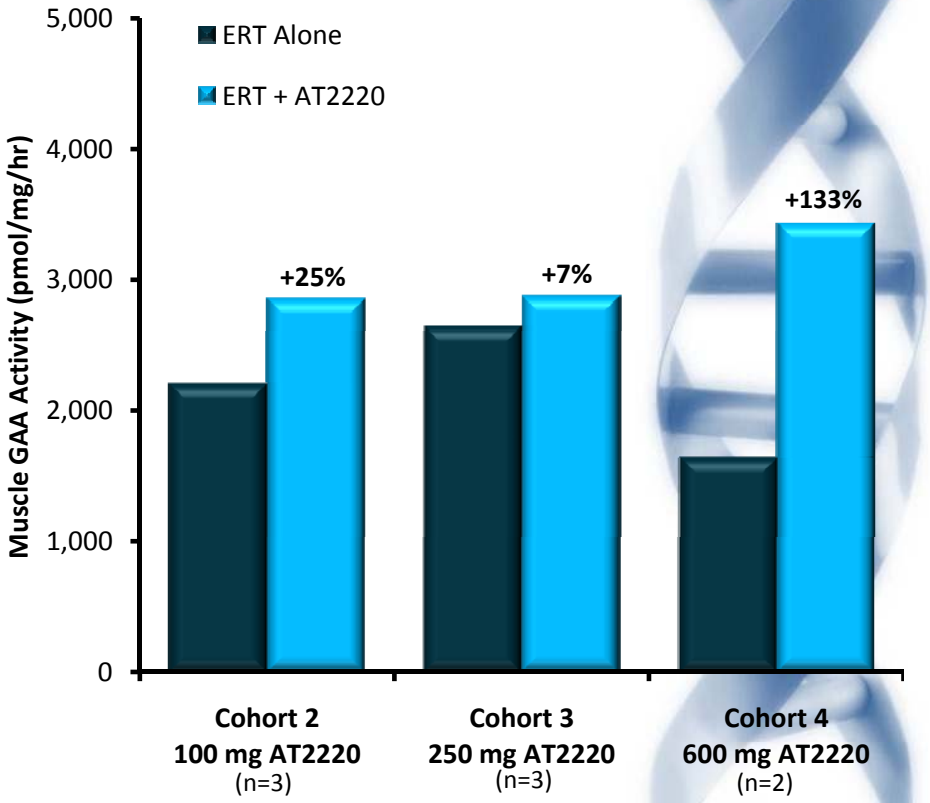
Phase 2 Study 010: Cohorts 1-4

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

Plasma AUC rhGAA Activity



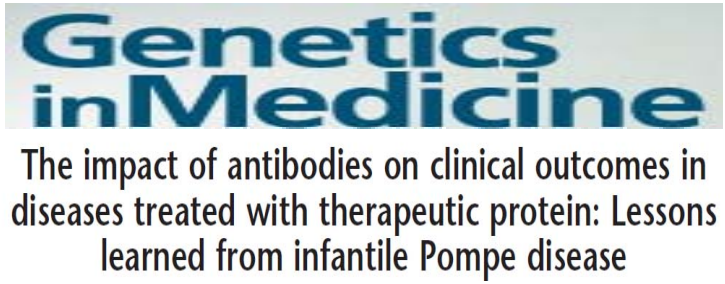
Muscle GAA Activity (Day 3)*



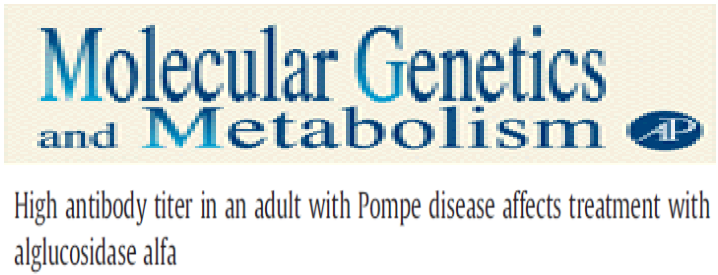
*Cohort 1 (AT2220 50 mg) muscle GAA activity not shown; 50 mg dose did not demonstrate meaningful change in tissue uptake (muscle)

Pompe Chaperone-ERT Co-Administration

ERT-Related Immunogenicity Problem



"…. identification of patients at risk for developing high sustained antibody titer is critical."[1]



"…. approximately 40% of the administered alglucosidase alfa was captured by circulating antibodies."[2]

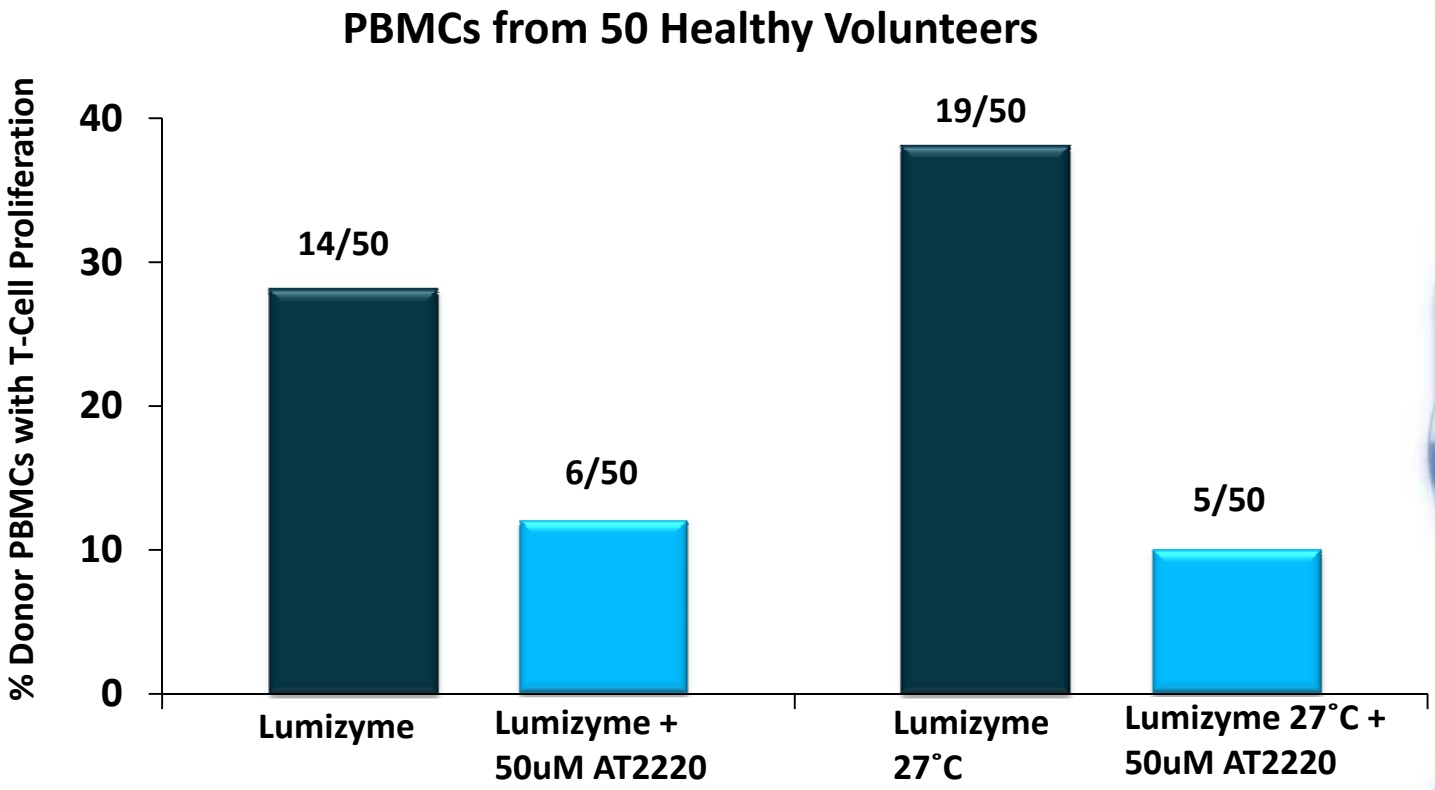
"…. infusion-associated reactions (IARs) [occur] in ~50% of patients receiving alglucosidase alfa infusions."[3]

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

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-Administration

Development Pathway

AT2220 IV Formulation

- Formulation complete
- GMP manufacturing underway
- Improved pharmacokinetic (PK) profile compared to oral AT2220
- Potential improved clinical benefits

AT2220 + ERT Co-Administration: Repeat-Dose Clinical Study

- Expected to begin 3Q13
- Target enrollment: adolescents/adults (ERT naïve and ERT experienced)
- Endpoints: PK, safety, efficacy and immunogenicity
- 12-24 week primary treatment period with potential extension

PHARMACOLOGICAL CHAPERONES

CO-FORMULATED WITH RECOMBINANT ERTS

TOWARD THE NEXT-GENERATION OF PROPRIETARY ERTS FOR LYSOSOMAL STORAGE DISORDERS

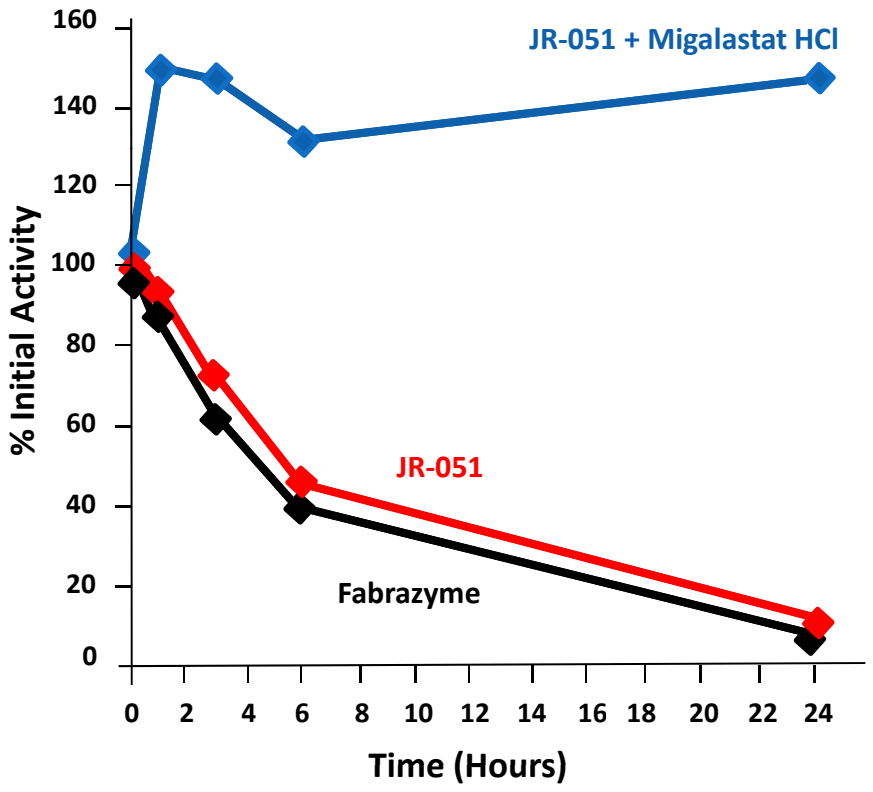
Fabry Chaperone-ERT Co-Formulation

Proprietary ERT JR-051 + Migalastat HCl*

Preliminary Results

Stabilization of JR-051 *ex vivo*

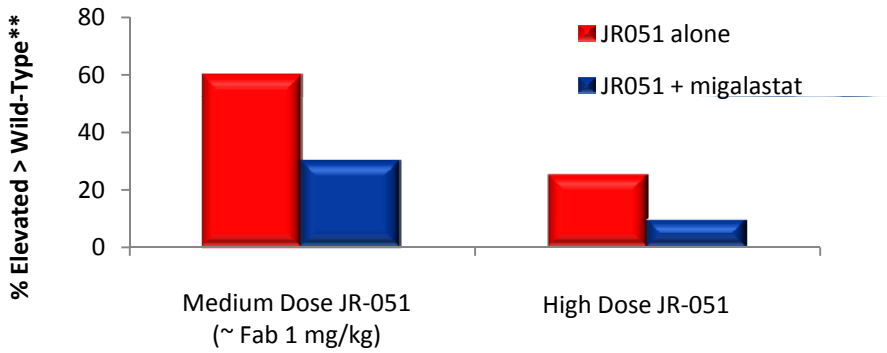
Migalastat HCl Prevents Loss of Enzyme Activity in Blood



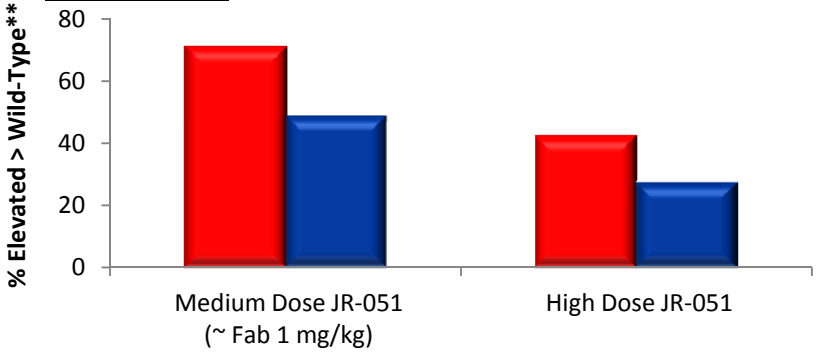
JR-051 +/- Migalastat HCl in GLA Knock-Out Mice (Repeat-Dose IV Administration)

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

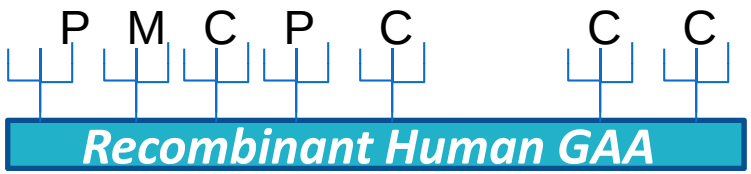
- Now manufacturing at 2,000 L scale
- IND-enabling studies underway
- Potential to enter clinic 4Q13/1Q14

Pompe Chaperone-ERT Co-Formulation

Next-Generation ERT for Pompe

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

Next-Generation Pompe ERT



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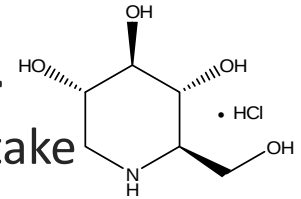
AT2220 Small Molecule Stabilizer



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

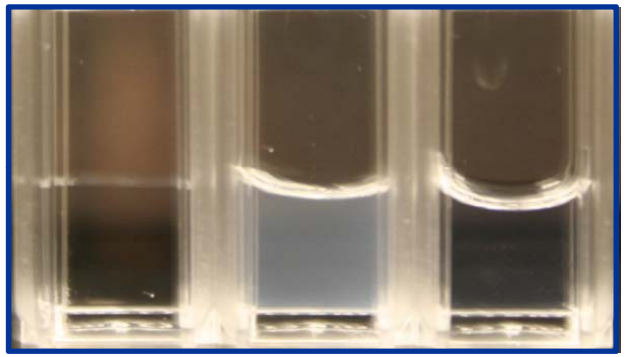
Potential Improvements

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

Pompe Chaperone-ERT Co-Formulation

Next-Generation ERT: SubQ Delivery Potential

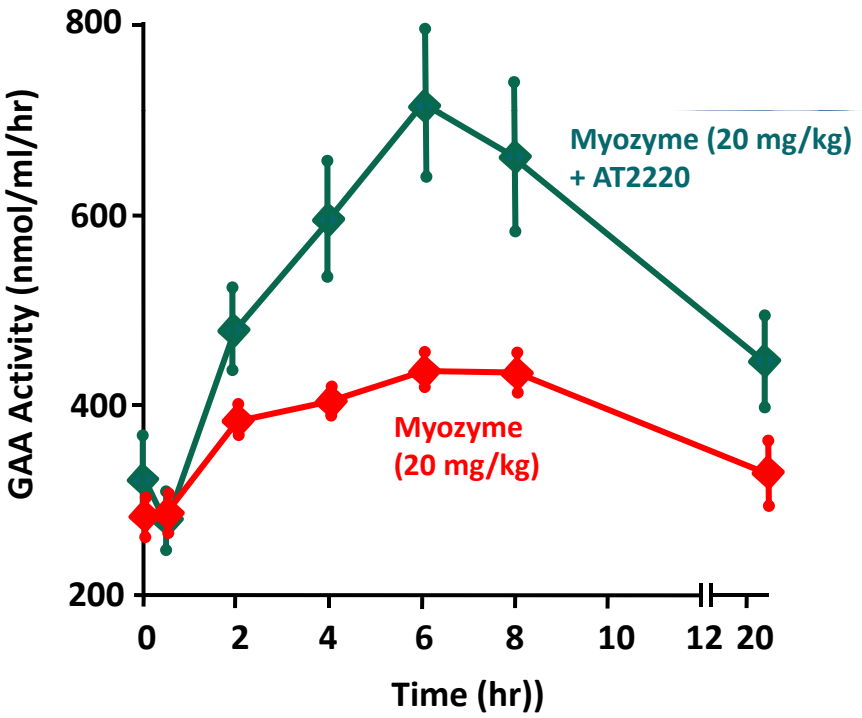
Increased ERT Stability and Prevention of Aggregation



Myozyme	-	+	+
AT2220	-	-	+

- Aggregation assessed after 4 weeks at 37˚C

Increased Circulating Levels of Active rhGAA in Rats



2013 KEY MILESTONES AND CATALYSTS

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