#### UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

#### FORM 8-K

CURRENT REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): May 19, 2015

#### AMICUS THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

001-33497

(Commission File Number)

71-0869350 (IRS Employer Identification No.)

> 08512 (Zip Code)

**1 Cedar Brook Drive, Cranbury, NJ** (Address of Principal Executive Offices)

Registrant's telephone number, including area code: (609) 662-2000

(Former Name or Former Address, if Changed Since Last Report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

#### Item 8.01 — Other Events.

The senior management of Amicus Therapeutics, Inc. (the "Company") is using the presentation attached as Exhibit 99.1 to this Current Report in its current meetings with investors and analysts.

2

#### Item 9.01. Financial Statements and Exhibits.

(d) Exhibits: The Exhibit Index annexed hereto is incorporated herein by reference.

Exhibit Number	Description
99.1	Presentation Materials
	3

#### SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Amicus Therapeutics, Inc.

By:

/s/ WILLIAM D. BAIRD III William D. Baird III Chief Financial Officer

4

#### EXHIBIT INDEX

Exhibit Number	Description
99.1	Presentation Materials
	5



## **Corporate Overview**

May 2015

at the forefront of therapies for rare and orphan diseases

## 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, cash runway, and 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' forwardlooking statements due to numerous known and unknown risks and uncertainties, including the "Risk Factors" described in our Annual Report on Form 10-K for the year ended December 31, 2014. 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 nextgeneration medicines to treat a range of rare and orphan diseases, with a focus on improved therapies for Lysosomal Storage Disorders



## **Amicus Value Proposition**

Building a Leading Global Rare Disease Company to Transform Lysosomal Storage Disease (LSD) Treatment Paradigm

Fabry franchise, led by novel pre-commercial oral medicine for patients with amenable mutations

Next-generation preclinical Pompe ERT to improve significantly uptake and tolerability

Multiple platform technologies to address current ERT limitations

Financial strength to develop and deliver improved therapies to patients

**Experienced Leadership team** 



# **Advanced Product Pipeline**

PRODUCT/PLATFORM	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	Regulatory
Fabry Franchise						
	Precision Me	dicine Monothera	эру			
<b>Migalastat</b> Pharmacological Chaperone Monotherapy & Combination w/ ERT	Co-Administr	ation with ERT		CHART	)	
	Next-Gen ER	CHART				
Pompe						
Next-Generation ERT ATB200 (rhGAA) + Chaperone			CHART			
MPS 1						
Next-Generation ERT		CHART				
	1					Am

## Amicus R&D Engine: Multiple Technology Platforms





# **Fabry Franchise**

## Fabry Disease Overview



## Chaperone Monotherapy: Precision Medicine Approach

Unique Mechanism of Action with Orally Bioavailable, Precision Medicine Small Molecule for Fabry Patients with Amenable Mutations



## **Fabry Franchise**

Migalastat is Designed to Stabilize a Patient's Own Enzyme or an Infused ERT



0

## Migalastat Monotherapy Experience for Fabry

#### 91 Patients Today Take Migalastat as Only Therapy for Fabry Disease\*



## **Two Successful Global Registration Studies**

Positive Results Support Global Approvals of Migalastat for Patients with Amenable Mutations



**Data** in ERT-naïve (Study 011) and ERT switch (Study 012) patients show:

Reduction in disease substrate

Stability of kidney function

Reduction in cardiac mass (LVMi)

Improvement in gastrointestinal symptoms

Generally safe and well tolerated

Marketing submissions planned in 2015



## Phase 3 (Study 011) Primary Efficacy Analysis

#### Statistically Significant Reduction in Disease Substrate (Kidney IC GL-3)\*



"All patients with evaluable paired biopsies and amenable GLA mutations in GLP-validated HEX assay – post hoc at month 6 and pre-specified at month 12 "Data points are baseline corrected; represent mean ± standard error (SEM) change from baseline in the mean number of GL-3 inclusions per capillary after 6 months of treatment with migalastat or placebo. <sup>2</sup>Analysis of covariance (ANCOVA) model with covariate adjustment for baseline value and factors for treatment group and treatment by baseline interaction. P-value corresponding to least-square mean difference between migalastat and placebo is displayed. <sup>3</sup>MMRM Pbo change M6 to M12.

## Phase 3 (Study 012) Primary Efficacy Analysis

Met Co-Primary Endpoints Showing Comparability of Kidney Function in Patients Switched from ERT to Migalastat

Annualized Rate of Change in eGFR and mGFR at Month 18 (ml/min/1.73 m<sup>2</sup>) 4 4 Difference = +0.63 Difference = -1.11 2 2 0 0 Δ = -0.40 Δ = -1.03 eGFR (CKD-EPI) mGFR -2 -2 Δ = -3.24 -4 -4 Δ = -4.35 -6 -6 -8 -8 -10 -10 Migalastat ERT Migalastat ERT n=34 n=18 n=34 n=18

- Amicus

14 <sup>1</sup> ANCOVA model [mITT]. Data represent LS means and 95% confidence intervals

## Phase 3 (Study 012) Cardiac Data

#### Reductions in LVMi Observed in Patients Switched from ERT Through Month 18 \*



Amicus

\*Mean change to month 18 (mITT; amenable mutations) \*\*Statistically significant (95% CI does not overlap zero)

Note: Mean and 95% confidence intervals on change from baseline are plotted

## Phase 3 (Study 011+041) Cardiac Data

#### New Data Show Migalastat Has Persistent and Increasing Positive Effect on LVMi Over Longer Periods of Time (Up to 36 Months)



\*Mean change to last available time point (average 22 months) in all patients with amenable mutations with baseline and post-baseline values. \*\*Statistically significant (95% CI does not overlap zero)

Sample size differences due to subjects not yet reaching a given timepoint or due to missing Echos

16 Note: Mean and 95% confidence intervals on change from baseline are plotted



## Phase 3 (Study 011) Patient-Reported Outcomes

#### Significant Reduction in Diarrhea Reported with Migalastat vs. Placebo at Month 6 was Persistent and Durable Through Month 24



## Phase 3 (Study 011) Patient-Reported Outcomes

#### Improvements in Indigestion and Favorable Trends in Reflux and Constipation Also Observed with Migalastat

	Gastrointestinal Symptoms Rating Scale									
GSRS Domain	Diarrh	iea	Reflu	х	Indiges	tion	Constip	ation	Abdomin	al Pain
Treatment Group	Migalastat	Placebo	Migalastat	Placebo	Migalastat	Placebo	Migalastat	Placebo	Migalastat	Placebo
			Ba	seline Valu	es: Mean (n)					
All Patients	2.3 (28)	2.1 (22)	1.4 (28)	1.4 (22)	2.5 (28)	2.4 (22)	1.9 (28)	2.0 (22)	2.1 (28)	2.3 (22)
Pts with BL Symptoms	3.2 (17)	3.1 (11)	2.1 (10)	2.6 (6)	2.8 (23)	2.7 (19)	2.5 (17)	2.4 (15)	2.4 (22)	2.9 (15)
		Char	nge from Base	line to Mo	nth 6 (Stage 1	, Double B	lind)			
All Patients	-0.3*	+0.2	-0.1	+0.2	-0.1	-0.1	+0.1	+0.2	0.0	0.0
Pts with BL Symptoms	-0.6	+0.2	-0.6*	+0.6	-0.2	-0.2	+0.2	+0.1	-0.1	-0.1
Change from Baseline (Migalastat) or Month 6 (Placebo) to Month 24 (Open-Label Extension Migalastat Treatment)										
All Patients	-0.5 (-0.9,	-0.1)**	-0.2 (-0.5	i, 0.2)	-0.4 (-0.7, -	-0.04)**	-0.4 (-0.7	, 0.0)	-0.2 (-0.5,	, +0.1)
Pts with BL Symptoms	-1.0 (-1.5,	-0.4)**	-0.6 (-1.5	i, 0.2)	-0.5 (-0.8, -	0.06)**	-0.5 (-1.1	, 0.0)	-0.2 (-0.6	, 0.1)

\*p≤0.05 based on ANCOVA; \*\*Statistically significant based on 95% CIs. LS Means shown for change from baseline

Amicus Therapeutics

## Phase 3 Validation of Personalized Medicine Approach

#### Lyso-Gb3 Data Validate Pharmacogenetic Approach to Identify Patients Who Respond to Migalastat



Amicus

<sup>1</sup>Hamler, et al., WORLDSymposium<sup>™</sup> 2015

## **Global Regulatory Strategy**



#### Global Fabry Market Exceeded \$1.1B in FY14 and Tracking Toward \$2B by 2021



- Fabry ERT sales increased 13.8% in 2014, continuing trend of double-digit annual growth<sup>1</sup>
- U.S. and Western Europe KOLs expect continued market growth:

"The number of diagnosed patients will increase. We keep identifying new patients, and this number is not decreasing year on year. I would not be surprised if it gets close to doubling in next 10 years" – UK Fabry KOL





## Migalastat Commercial Opportunity

#### **Attractive Commercial Opportunity with Significant Number of Amenable Patients**



#### Large Number of Patients Identified Through Newborn Screening Suggests Fabry Could Be One of the More Prevalent Human Genetic Diseases

Newborn Screening Study	# Newborns Screened	# Confirmed Fabry Mutations	% 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%
Historic published incider	nce	1:40,000 to 1	60,000

#### Majority Diagnosed through Newborn Screening Have Amenable Mutations

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





## Positive KOL Feedback

Based on Target Product Profile, KOLs Would Use Migalastat in Most Naïve and Switch Patients with Amenable Mutations with Signs and Symptoms if Approved



## Payor Feedback Supports Reimbursement

#### Interviews with 20 Payors in Major Markets Suggest **Broad Reimbursement and Coverage for Amenable Patients if Approved** Based on Target Product Profile, payors interviewed in all studied Coverage countries believe there is sufficient evidence to support reimbursement supported by clinical trial data... of migalastat "... I think the level of evidence is good enough here for reimbursement, at least at [pricing] parity to ERT ... " Payor, UK Additionally, assuming parity pricing to ERT, payors generally expressed ...and more high interest in including migalastat in their formulary as they believe convenient route of most patients would prefer oral route of administration over infusion administration "... If it was priced at parity with ERT, there would be zero restrictions on its use ..." Payor, U.S.

Source: third party payor interviews and analysis

25



## **Global Pre-Commercial Activities**

#### Amicus is Building on Global Migalastat Experience to Prepare for Successful Launch



- Hiring experienced team
- European headquarters selected
- Medical outreach underway
- Patient advocacy ongoing
- Access and reimbursement
- Designing product experience





#### Our Vision is to Treat All Fabry Patients with an Amicus Product if Approved



# Key Milestones – Fabry Franchise

Timing	Milestone	
1Q15	Additional 011 and Phase 2 extension data	$\checkmark$
1Q15	Scientific Presentations at LDN WORLD	$\checkmark$
1Q15	US and EU Regulatory Interaction	$\checkmark$
2Q15	MAA Submission	
2H15	NDA Submission	
2H15	Phase 2 Co-Administration Study Initiation	
2H15	Internal Development of Next-Gen ERT Cell Line	

![](_page_30_Picture_0.jpeg)

## Pompe Disease Overview

Severe, Fatal, Progressive Neuromuscular Disease with Significant Unmet Need Despite Availability of ERT

![](_page_31_Picture_2.jpeg)

## Select Milestones in Pompe Drug Development

A Decade After Initial Clinical Studies of Myozyme<sup>®</sup>, Researchers Still Working to Develop Next-Generation Treatment for Pompe Patients

![](_page_32_Figure_2.jpeg)

## **Current Pompe ERT Limitations**

#### Significant Unmet Needs Remain Due to Limitations of First-Generation Pompe ERT

"...Biologic drugs, including enzyme-replacement therapies, can elicit anti-drug Abs (ADA) that may interfere with drug efficacy and impact patient safety." (Journal of Immun. 2014) "...recurrent injections of rhGAA during ERT can elicit high titer antibody formation against GAA; this reduces the efficacy of ERT and may prompt infusion associated reactions (IAR) that may be lifethreatening." (Doerfler, et al. WORLD 2014)

Pediatric RESEARCH

"All 18 patients who enrolled in the initial [infantile-onset Pompe] study survived significantly longer and with fewer ventilation events ... However, morbidity and mortality remain substantial, with a 28% mortality rate and a 51% invasive ventilation rate at age 36 months." (Kishnani, et al. 2009)

#### The NEW ENGLAND JOURNAL of MEDICINE

"...14% of pts on [Lumizyme] treatment have declining 6-minute walk test and 36% have declining forced vital capacity." (van der Ploeg, et al. 2010)

![](_page_33_Picture_8.jpeg)

## Three Challenges with Pompe ERT Today

Activity/ Stability

Rapid denaturation of ERT in pH of blood<sup>1</sup>

of Protein Aggregation

#### Tolerability / Immunogenicity

Infusion-associated reactions in >50% of late-onset patients<sup>3</sup> Antibody titers shown to affect treatment outcomes<sup>4,5</sup>

#### Uptake/ Targeting

Low M6P receptor uptake into skeletal muscle<sup>2</sup> Vast majority of rhGAA not delivered to lysosomes<sup>2</sup>

Amicus

<sup>1</sup>Khanna et al., PLoS ONE, 2012; <sup>2</sup>Zhu et al., Amer. Soc. Gene Therapy, 2009 June; <sup>3</sup>Banati et al., Muscle Nerve, 2011 Dec.; <sup>4</sup>Banugaria et al., Gen. Med., 2011 Aug.; <sup>5</sup>de Vries et al., Mol Genet Metab., 2010 Dec.

## **Amicus Biologics Platform Technologies**

#### Multiple Complementary Amicus Platform Technologies With Potential to Address The Challenges with Existing ERTs Today

![](_page_35_Figure_2.jpeg)

### Human Proof-of-Concept: Currently Marketed ERT + Chaperone

Investigator-Initiated Study Demonstrates Profound Effect of Chaperone Co-Administered with Pompe ERT

Two Pompe patients could not tolerate ERT infusions

Investigator re-initiated ERT with oral co-administration of pharmacological chaperone

The two Pompe patients now able to fully tolerate ERTs

Amicus

## Human Proof-of-Concept: Currently Marketed ERT + Chaperones

#### ERT Activity Increased and Infusion Time Decreased with Chaperones\*

![](_page_37_Figure_2.jpeg)

Kishnani, et al., LDN WORLD 2013

<sup>2</sup>Doerfler, et al. WORLD 2014 \*Cohort 1 (AT2220 50 mg) muscle GAA activity not shown; 50 mg dose did not demonstrate meaningful change in tissue uptake (muscle)

Amicus Therapeutics

## ATB200 Preclinical Proof-of-Concept

#### Higher bis-M6P N-Glycan Content on ATB200 Directly Correlated with High-Affinity Binding to CIMPR in M6P Receptor Plate Binding Assays (KD~2-4 nM)

30

GAA Activity (nmol 4MUreleased/mL/hr)

> 0<del>1</del> 0.1

# GlycanLumizyme<br/>(mol bis-<br/>glycan/mol<br/>protein)ATB200<br/>(mol/bis-<br/>glycan/mol protein)Bis-M6P0.11.3

**Bis-Phosphorylated Glycan Analysis** 

CIMPR Binding Affinity

10

1

![](_page_38_Picture_4.jpeg)

ATB200 Lumizyme

1000

100

![](_page_38_Picture_5.jpeg)

## ATB200 + Chaperone Preclinical Proof-of-Concept

#### ATB200 + Chaperone Reduced Skeletal Muscle Glycogen to Near Normal Levels in Gaa KO Mice

![](_page_39_Figure_2.jpeg)

Two IV bolus administrations of ERT (every other week ). Pharmacological chaperone administered orally 30 min prior to ERT. Tissues harvested 2 weeks after last dose. Tissues analyzed for GAA activity and glycogen content

![](_page_39_Picture_4.jpeg)

#### After Two Doses - Glycogen Clearance Correlates with Endocytic Vesicle Turnover in Skeletal Muscle

PAS- glycogen staining in Quadriceps

![](_page_40_Picture_3.jpeg)

Untreated

![](_page_40_Picture_4.jpeg)

![](_page_40_Picture_5.jpeg)

ATB200

![](_page_40_Picture_6.jpeg)

ATB200+ AT2221

![](_page_40_Picture_7.jpeg)

Untreated Alglucosidase Alfa LAMP1 Immunohistochemical staining in Soleus

![](_page_40_Picture_9.jpeg)

![](_page_40_Picture_11.jpeg)

Alglucosidase Alfa

ATB200+ AT2221

w

 Following 2 doses of 20mg/kg Alglucosidase Alfa and ATB200 +/- AT2221 in Gaa KO mice, skeletal muscle evaluated for glycogen clearance and lysosomes

ATB200

- Treatment with ATB200 resulted in greater glycogen reduction and improved muscle physiology
- Co-administration of ATB200 with AT2221 had an even greater impact on decreasing the muscle pathology associated with Pompe disease.

![](_page_40_Picture_19.jpeg)

## **Amicus Biologics Capabilities**

ATB200 Successfully Manufactured at Clinical Scale While Maintaining Optimized Carbohydrate Structure

![](_page_41_Picture_2.jpeg)

- Cell line scaled to 250 L
- 2 engineering batches completed in 2014
- IND-enabling tox underway

![](_page_41_Picture_6.jpeg)

## Amicus Pompe ERT: Highly Differentiated Approach

#### Amicus to advance ATB200 + Chaperone into Phase 1/2 in 2015 Potential Solution for Key ERT Limitations

Pompe ERT Challenges	IGF2-GAA	IGF2-GAA Neo-GAA	
Stability & Activity			V (Chaperone)
Targeting & Uptake	(IGF2 Tag)	✓ (М6Р)	M6P, Chaperone)
Tolerability & Immunogenicity			✓ (Chaperone)
Development Stage	Phase 2	Phase 1	Late Preclinical

✓ = May address

![](_page_42_Picture_4.jpeg)

# Pompe: Multiple Milestones to Clinic

Timing	Milestone
1Q15	Initiate GMP Batch
3Q15	Tox Studies
Mid-2015	Pre-IND Meeting
2H15	Phase 1/2 study initiation

![](_page_43_Picture_2.jpeg)

![](_page_44_Picture_0.jpeg)

# **Financial Summary**

Financial Summary

Strong Balance Sheet to Fund Operations into 2H16

Financial Position	Mar. 31, 2015
Cash:	\$151.6M
2015 Net Cash Spend Guidance:	\$100M-110M
Capitalization	
Shares Outstanding:	96.4M

![](_page_45_Picture_3.jpeg)