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 14, 2019**

AMICUS THERAPEUTICS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**001-33497**	**71-0869350**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

1 Cedar Brook Drive, Cranbury, NJ 08512
(Address of Principal Executive Offices, and Zip Code)

609-662-2000
Registrant's Telephone Number, Including Area Code

(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))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 Par Value	FOLD	NASDAQ

Item 8.01. Other Events

On May 14, 2019, Amicus Therapeutics, Inc. updated and released presentation materials it plans to use in connection with its presentation at Bank of America Merrill Lynch 2019 Health Care Conference. A copy of this presentation is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

Exhibits:

Exhibit No.	Description
99.1	Corporate Presentation - Bank of America Merrill Lynch 2019 Health Care Conference

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.

Date: May 14, 2019

AMICUS THERAPEUTICS, INC.
By: /s/ Ellen S. Rosenberg
Name: Ellen S. Rosenberg
Title: Chief Legal Officer and Corporate Secretary

Amicus Therapeutics®

Corporate Overview

May 2019

Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 rela preclinical and clinical development of our product candidates, the timing and reporting of results from preclinical studies and clinical tr prospects and timing of the potential regulatory approval of our product candidates, commercialization plans, manufacturing and supply financing plans, and the projected revenues and cash position for the Company. The inclusion of forward-looking statements should not be re as a representation by us that any of our plans will be achieved. Any or all of the forward-looking statements in this press release may turn o wrong and can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. For example, with re statements regarding the goals, progress, timing, and outcomes of discussions with regulatory authorities, and in particular the potentia progress, timing, and results of preclinical studies and clinical trials, actual results may differ materially from those set forth in this release du risks and uncertainties inherent in our business, including, without limitation: the potential that results of clinical or preclinical studies indica the product candidates are unsafe or ineffective; the potential that it may be difficult to enroll patients in our clinical trials; the potent regulatory authorities, including the FDA, EMA, and PMDA, may not grant or may delay approval for our product candidates; the potential may not be successful in commercializing Galafold in Europe, Japan, the US and other geographies or our other product candidates if an approved; the potential that preclinical and clinical studies could be delayed because we identify serious side effects or other safety issu potential that we may not be able to manufacture or supply sufficient clinical or commercial products; and the potential that we will need ad funding to complete all of our studies and manufacturing. Further, the results of earlier preclinical studies and/or clinical trials may not be pr of future results. With respect to statements regarding projections of the Company's revenue and cash position, actual results may differ b market factors and the Company's ability to execute its operational and budget plans. In addition, all forward-looking statements are subject t risks detailed in our Annual Report on Form 10-K for the year ended December 31, 2018. You are cautioned not to place undue reliance o forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cau statement, and we undertake no obligation to revise or update this news release to reflect events or circumstances after the date hereof.

Amicus Highlights

GALAFOLD'S EXTRAORDINARY LAUNCH SUCCESS

- 650+ Patients and $91.2M Global Sales in FY18
- FY19 Guidance of $160M-$180M
- $500M Potential Sales by 2023
- $1B+ Addressable Market Opportunity by 2028

AT-GAA IN POMPE: POTENTIAL TO BECOME STANDARD OF CARE

- Continued Strength of Clinical Data
- Granted Breakthrough Therapy Designation
- Multiple Data Expected Throughout 2019
- 100+ Pompe Patients on AT-GAA by YE19
- $1B-$2B+ Market Opportunity

LEADING GENE THERAPY PORTFOLIO METABOLIC DISEASES

- Pipeline of 14 Gene Therapies
- 2 Clinical Stage Programs
- Established Global Research and Gene Th Center of Excellence in Philadelphia
- $1B+ Peak Recurring Market Opportunity

FINANCIAL STRENGTH

- $500M+ Cash at 12/31/18 (runway into mid-2021)
- Growing Contribution from Galafold Revenues

2023 VISION

- 5,000+ Lives Transformed
- $1B+ in Revenue
- Leading Global Rare Disease Biotech

Amicus Founding Beliefs

We push ideas as far and as fast as possible

We encourage and embrace constant innovation

We have a duty to obsolete our own technologies

We are business led and science driven

Our passion for making a difference unites us

WE BELIEVE...

In the Fight to Remain at the F[illegible] Therapies for Rare and Orphan Diseases

- We seek to deliver the highest quality therapies for persons living with these diseases
- We support t[illegible]
- We are passionate about what we do
- We encourage and embrace constant innovation
- We have a duty to obsolete our own technologies
- We push ideas as far and [illegible]
- We take smart risks
- We work hard
- We keep asking the tough questions
- We will never be c[illegible]strained by prior thinking
- We learn from our [illegible]
- We think differently - very differently

WE BELIEVE...

In Our Future to Build [illegible] Our Stakeholders

- We are all owners of this business
- We are business led and science [illegible]
- Maximizing value for our shareholders is the foundation of our future successes
- [illegible] and broadly accessible
- We build strategic partnerships
- We will not lie, cheat or steal
- [illegible] actions

WE BELIEVE...

In Each Other to [illegible]mwork and Respect for Each **Individual's** Contribution

- Our passion for making a difference unites us
- [illegible]ce and thought is essential
- We communicate openly, honestly and respectfully
- [illegible]ilies are part of the Amicus experience
- Work-life balance keeps us healthy

A RARE COMPANY.

Galafold™ (migalastat)

First Oral Precision Medicine for Fabry Disease

BIOLOGICS PLATFORM

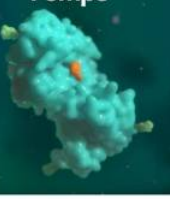
Protein Engineering & Glycobiology

$500M+ Cash (12/31/18)

Gene Therapy Platforms

AT-GAA*

Phase 3 Investigational Therapy for Pompe



500+ EMPLOYEES globally

GLOBAL FOOTPRINT in 27 countries

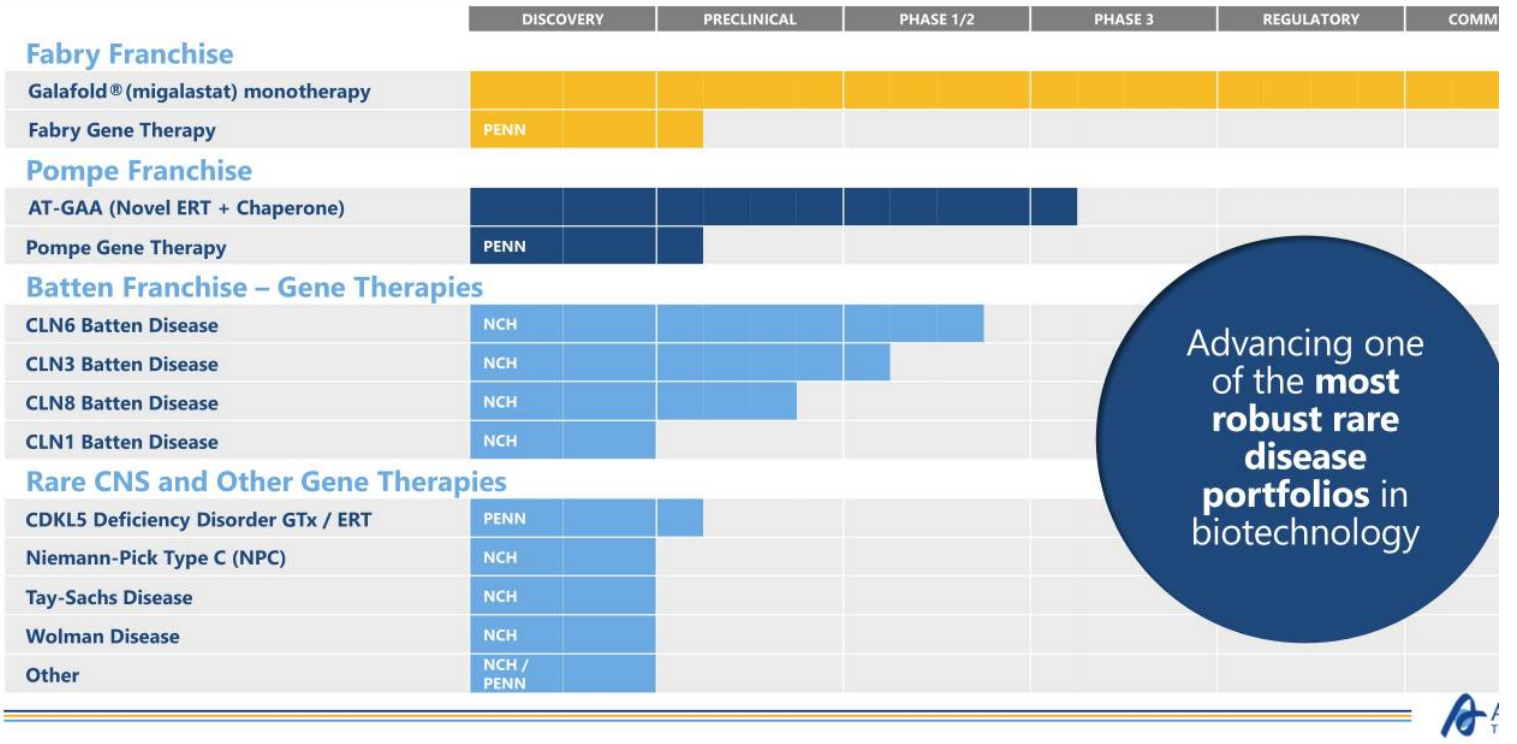
PORTFOLI

of 15 programs for r metabolic disease

Leading Expertise in **Lysosomal Storage Disorders**

* AT-GAA, also known as ATB200/AT2221

A RARE PORTFOLIO.



A RARE OPPORTUNITY.

Key Drivers of Value

***Transform* the Lives of Thousands of Patients**

2019 Key Strategic Priorities

1. **Nearly double annual revenue for Galafold (guidance $160M-$180M)**
2. **Complete enrollment in AT-GAA Pivotal Study (PROPEL) and report additional Phase 1/2 data**
3. **Report additional 2-year clinical results in CLN6-Batten disease and complete enrollment in ongoing CLN3-Batten disease Phase 1/2 study**
4. **Establish preclinical proof of concept for Fabry and Pompe gene therapies**
5. **Maintain strong financial position**

A RARE VISION. Impacting Lives

>350 Patients* | ~$36M Global Sales

>700 Patients* | ~$91M[1] Global Sales

5,000 Patients* | $1B Global Sa

YE17 → YE18 → 2023

*Clinical & commercial, all figures approximate [1]Preliminary unaudited

Amicus in 2023

Fabry Disease Overview

"We support the disease communities – and their ***families***

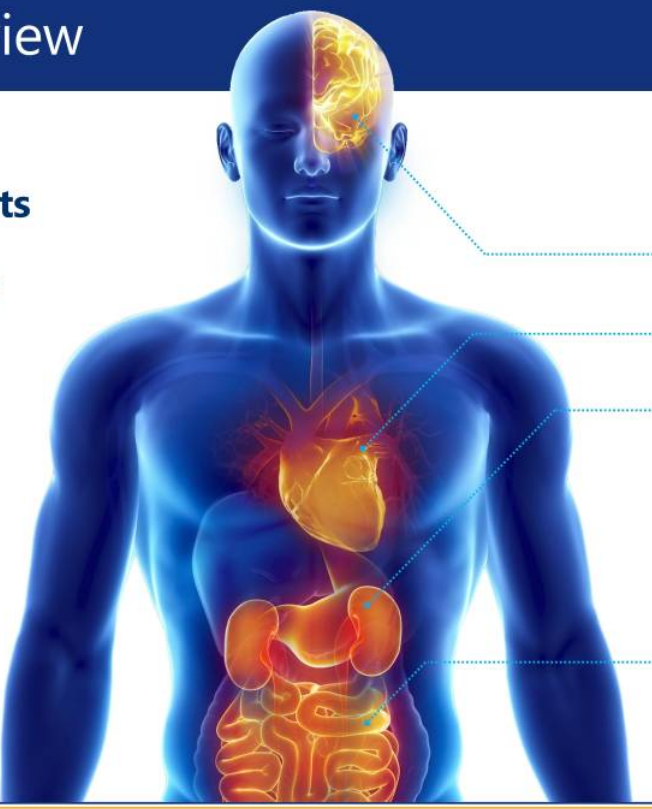
- Amicus Belief Statemer

Fabry Disease Overview

Fabry Disease is a Fatal Genetic Disorder that Affects Multiple Organs and is Believed to be Significantly Underdiagnosed

Key Facts:

- α-Gal A enzyme deficiency leads to substrate (GL-3) accumulation
- >1,000 known mutations
- ~10K diagnosed WW (51% female/49% male[4])
- Newborn screening studies suggest prevalence of ~1:1000 to ~1:4000



Leading Causes of Dea

- Transient Ischemic Attac (TIA) & Stroke[1]
- Heart Disease[2]
- Kidney Disease[3]

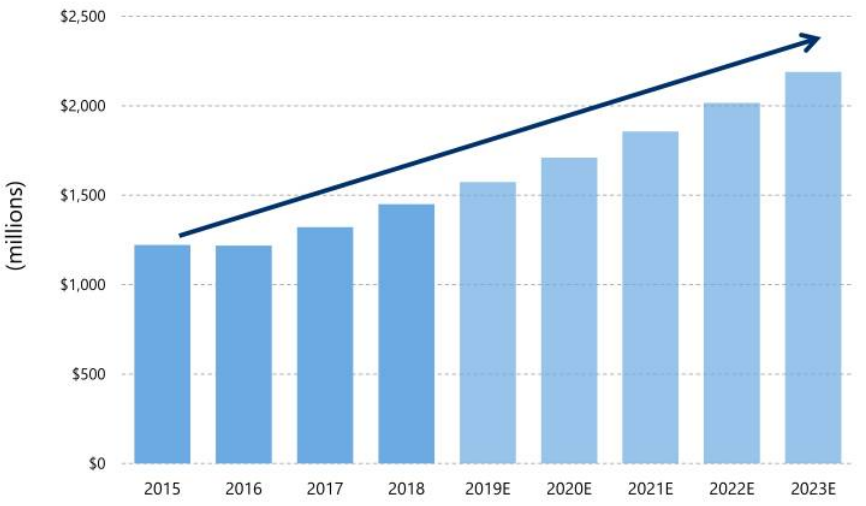
Life-Limiting Sympto

- Gastrointestinal[3]

1. Desnick R, *et al.* Ann Intern Med. 2003; 2. Yousef Z, *et al.* Eur Heart J. 2013; 3. Germain D. Orphanet J Rare Dis. 2010 4. Fabry Registry 2011

Global Fabry Market Growth Driven by New Patients

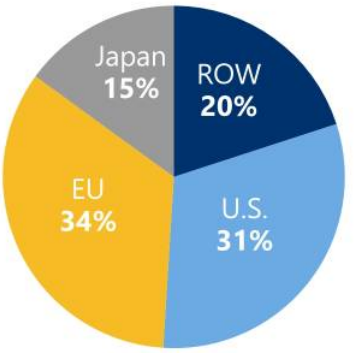
Global Fabry Market Exceeded $1.4B as of 3Q18 and Tracking Toward $2.2B by 2023 (8.6% 5-Year CAG



Global Fabry Market and growth measured by reported CER (constant exchange rates) Adjusted Net Sales through 3Q18
Δ 2018 – 2023 are based on estimated 8.6% annual growth rate (5-Year CAGR rate)

Annualized 3Q18 Fabry sales increased

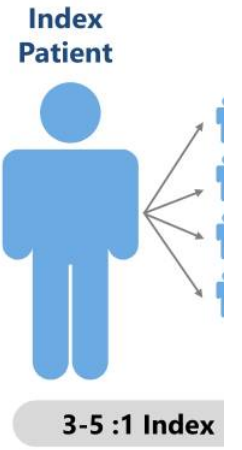
10%



Fabry Underdiagnosis

Newborn Screening Studies Suggests Fabry Could Be One of the More Prevalent Human Genetic Disea

NEWBORN 8454ENING STUDY	NEWBORNS SCREENED	CONFIRMED FABRY MUTATIONS	% AMENABLE
Hopkins, 2018, Missouri, US	43,701	15 [1:~2913]	N/A
Burton, 2017, Illinois, US	219,793	26 [1: ~8454]	N/A
Mechtler, 2011, Austria	34,736	9 [1: ~3800]	100%
Hwu, 2009, Taiwan	171,977	75 [1: ~2300]	N/A
Spada, 2006, Italy	37,104	12 [1: ~3100]	86%
Historic published incidence		**1:40,000 to 1:60,000**	

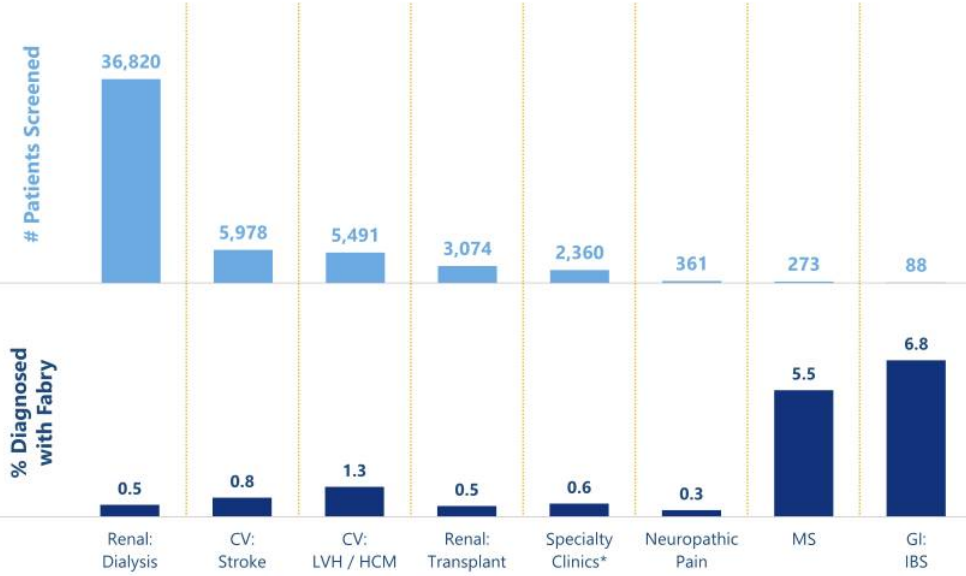


Majority Diagnosed through Newborn Screening Have Amenable Mutations

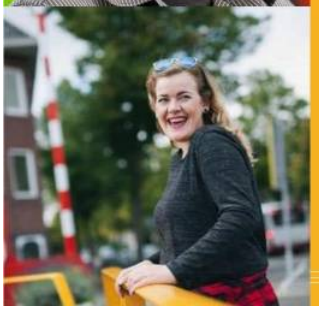
Burton 2017 J Pediatr 2017;190:130-5 ; Mechtler *et al.*, **The Lancet**, 2011 Dec. Hwu *et al.*, **Hum Mutation**, 2009 Jun; Spada *et al.*, **Am J Human Genet.**, 2006 Jul

Fabry Misdiagnosis

Recent Studies in Multiple Disease Areas Show Significant Rate of Fabry Disease as Underlying Caus



Source: Summary of N=63 completed high-risk screening associated studies, Huron Analysis *Specialty clinics include neurology, cardiology, nephrology, and pediatrics **1 MS completed study refers to % of FD patients misdiagnosed with MS



Galafold® (migalastat) Global Launch…

…taking a leadership role in the treatment of Fabry disease

"We push ideas as far and as fast as possible

- Amicus Belief Statemer

Galafold Snapshot (as of March 31, 2019)

One of the Most Successful Rare Disease Launches

$34.0M
1Q19 Galafold Revenue

$160-180M
FY19 Global Galafold Rev. Guidance

Geographic Expansion in 2019

Galafold™ (migalastat)

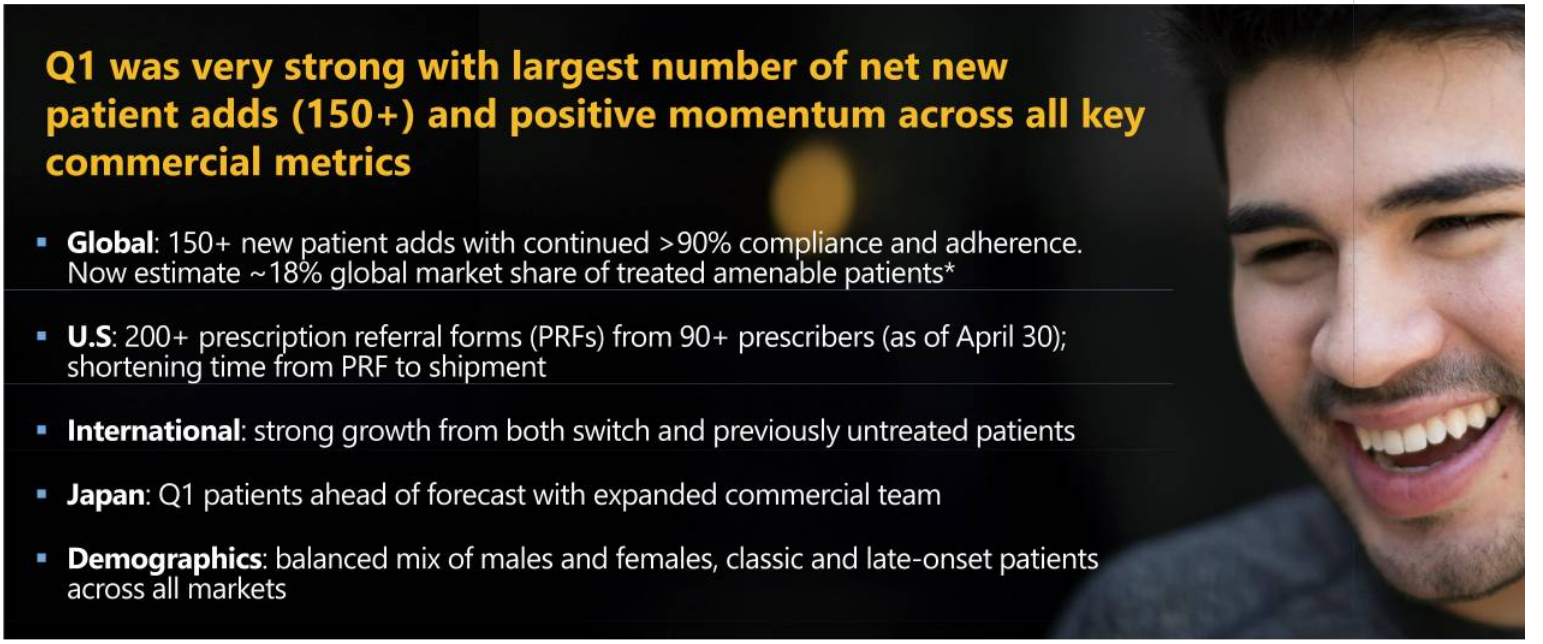
24
Countries with Pricing & Reimbursemen

8
Regulatory Approvals:
Australia, Canada, EU, Israel, Japan, S. Korea, Switzerland , U.S.

348
Amenable Variants in U.S. Label

Galafold is indicated for adults with a confirmed diagnosis of Fabry Disease and an amenable mutation/variant. The most common adverse reactions reported with Galafold (≥10%) were headache, nasopharyngitis, urinary tract infection, nausea and pyrexia. For additional information about Galafold, including the full U.S. Prescribing Information, please visit https://www.amicusrx.com/pi/Galafold.pdf. For further important safety information for Galafold, including posology and method of administration, special warnings, drug interactions and adverse drug reactions, please see the European SmPC for Galafold available from the EMA website at www.ema.europa.eu.

Galafold Global Launch Momentum (as of March 31, 2019)



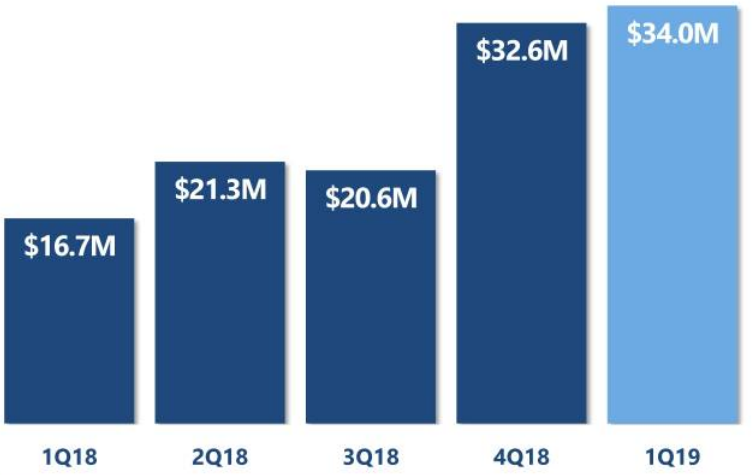
Q1 was very strong with largest number of net new patient adds (150+) and positive momentum across all key commercial metrics

- **Global**: 150+ new patient adds with continued >90% compliance and adherence. Now estimate ~18% global market share of treated amenable patients*
- **U.S**: 200+ prescription referral forms (PRFs) from 90+ prescribers (as of April 30); shortening time from PRF to shipment
- **International**: strong growth from both switch and previously untreated patients
- **Japan**: Q1 patients ahead of forecast with expanded commercial team
- **Demographics**: balanced mix of males and females, classic and late-onset patients across all markets

*Market share based on reported 2018 global Fabry sales and assumes a 35% amenability rate for Galafold.

Galafold Quarterly Performance

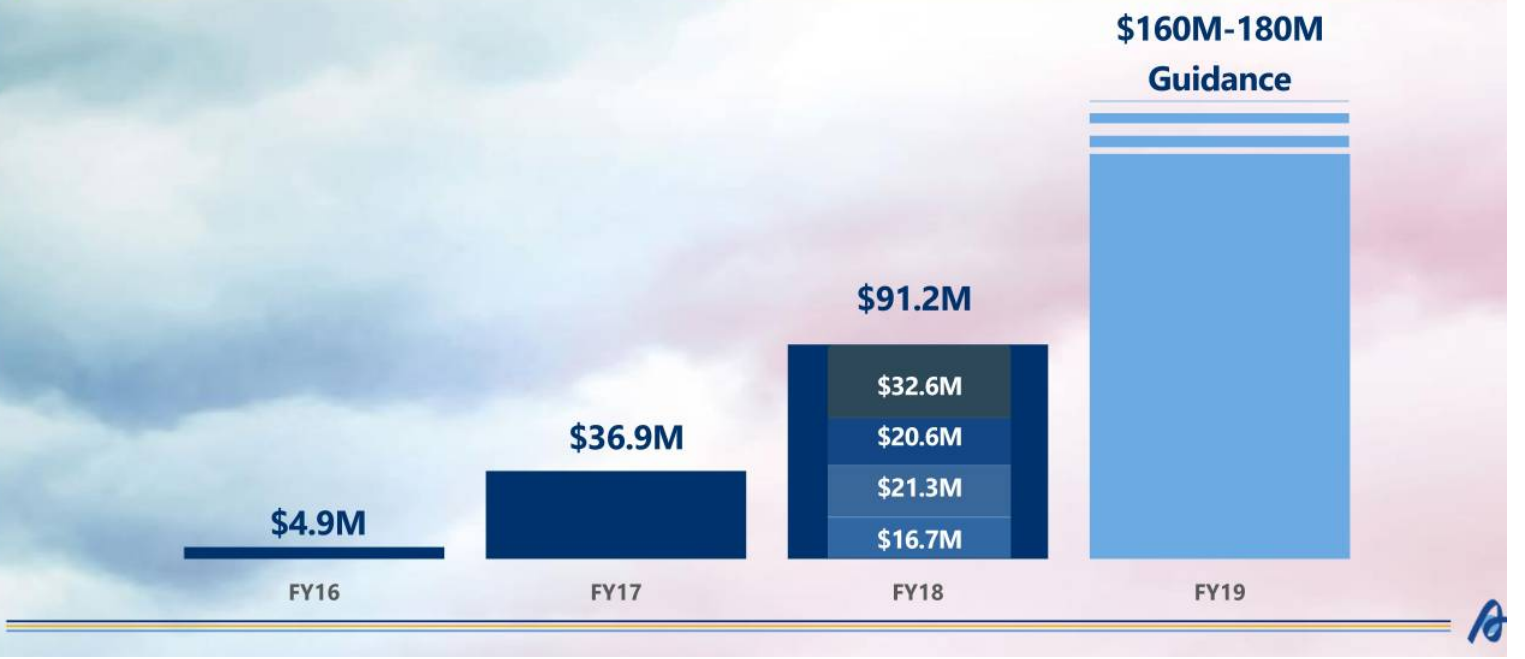
1Q19 Revenue of $34.0M Grew 104% Year-over-Year Reflecting Continued Stro
Growth in Global Adoption of First Fabry Oral Precision Medicine



- 1Q19 in-line with management expectations
- Consistent with Galafold adoption trends and ordering patterns in previous years, quarter to quarter growth will not be linear
- Strong start to 2Q19 ahead of management expectations
- Higher revenue growth expected in 2Q19 and 4Q19

Galafold Success and FY19 Galafold Revenue Guidance

On Track to Nearly DOUBLE Revenue Again and Serve 1,000+ Patients in 2019

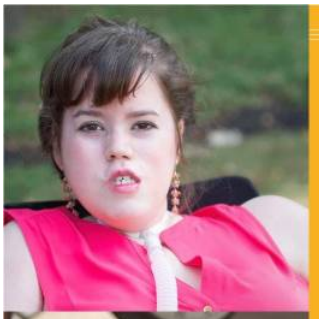


Total Amenable Patient Population ("TAPP")

Estimate based on 35% - 50% amenability

$1B+ Addressable Market Opportunity by 2028

*WORLDWIDE includes total amenable patient population in all Fabry ERT commercial markets today Estimated effect of newborn screening on adult diagnostic rate.



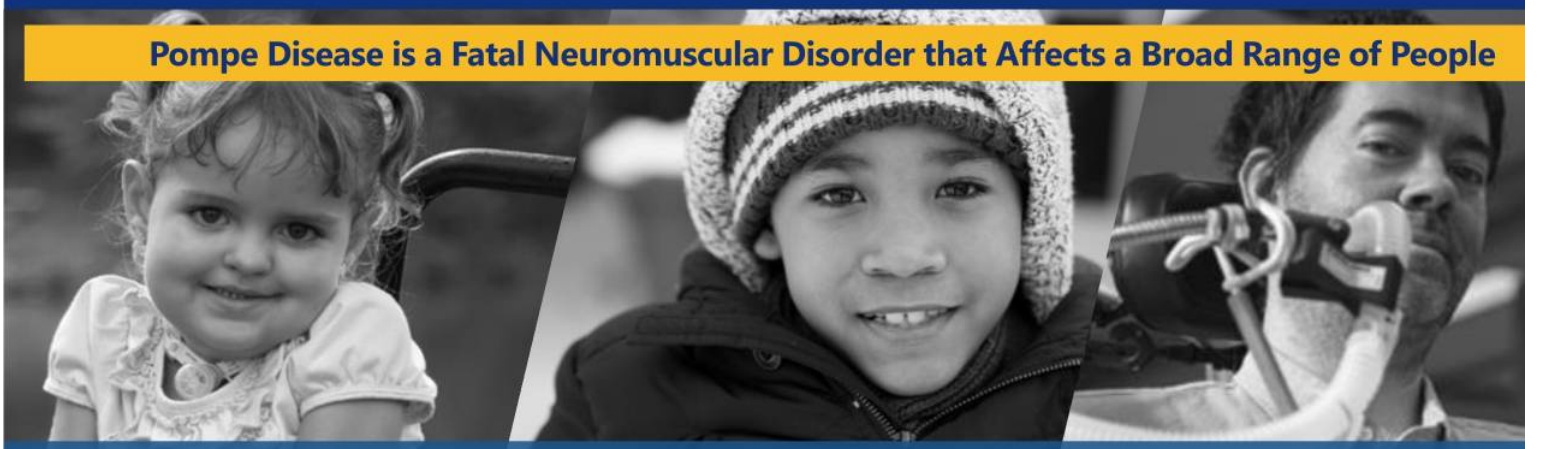
AT-GAA Novel ERT for Pompe Disease

"We encourage and embrace constant innovation

- Amicus Belief Statemer

Pompe Disease Overview

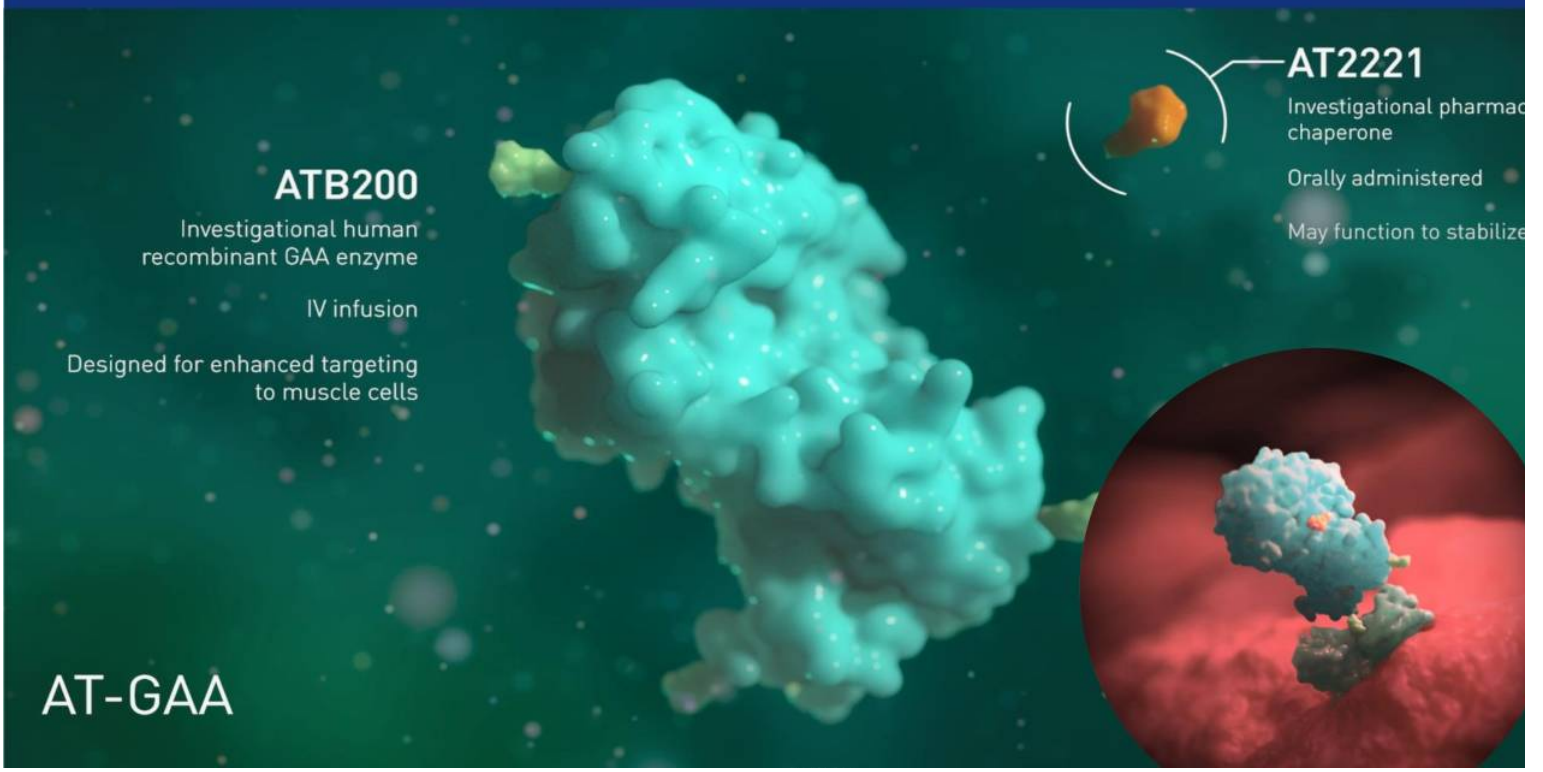
Pompe Disease is a Fatal Neuromuscular Disorder that Affects a Broad Range of People



- 5,000 – 10,000 patients diagnosed WW[1]
- Respiratory and cardiac failure are leading causes of morbidity and mortality
- Age of onset ranges from infancy to adulthood
- Deficiency of GAA leading to glycogen accumulation
- Symptoms include muscle weakness, respiratory failure, and cardiomyopathy
- ~$900M+ Global Pomp ERT sales in FY17[2]

1. National Institute of Neurological Disorders and Stroke (NIH). 2. Sanofi Press Release & 10-K

AT-GAA (ATB200 + Chaperone): A Differentiated Treatment Paradigr



Pompe Patient Experience in Phase 1/2 Clinical Study (ATB200-02)

Consistent and Durable Responses Across Key Measures of Safety, Functional Outcomes and Biomarkers in both ERT-Switch and ERT-Naïve Pompe Patients out to Month 18

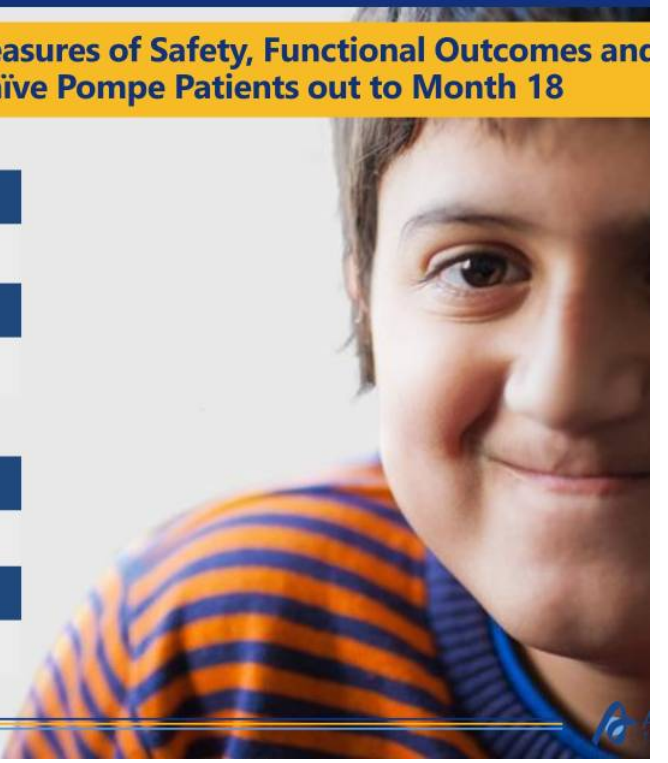
6-Minute Walk Test (m)

Cohort	Baseline (n=10)	Change at Month 24[a,b] (n=8) Mean (SD)
Cohort 1 ERT-Switch Ambulatory	**397.2** (96.8)	**+53.6** (36.4)
Cohort	**Baseline (n=5)**	**Change at Month 21 (n=5) Mean (SD)**
Cohort 3 ERT-Naïve	**399.5** (83.5)	**+54.8** (34.7)

FVC (% Predicted)

Cohort	Baseline (n=9*)	Change at Month 24[a,b,c] (n=7) Mean (SD)
Cohort 1 ERT-Switch Ambulatory*	**52.6** (14.7)	**-0.6** (2.8)
Cohort	**Baseline (n=5)**	**Change at Month 21 (n=5) Mean (SD)**
Cohort 3 ERT-Naïve	**53.4** (20.3)	**+6.1** (9.7)

[a]One patient in Cohort 1 discontinued from study (withdrew consent) before Month 24. [b]At the time of this interim analysis, 1 patient in Cohort 1 had not reached Month 24. [c]Baseline FVC missing for 1 patient in Cohort 1



AT-GAA: Breakthrough Therapy Designation

U.S. FDA Granted BTD to AT-GAA in Late-Onset Pompe Disease (LOPD)

BTD Criteria

- Intended to treat a serious or life threatening disease or condition
- Preliminary clinical evidence indicates drug may demonstrate substantial improvement over existing therapies on one or m clinically significant endpoints

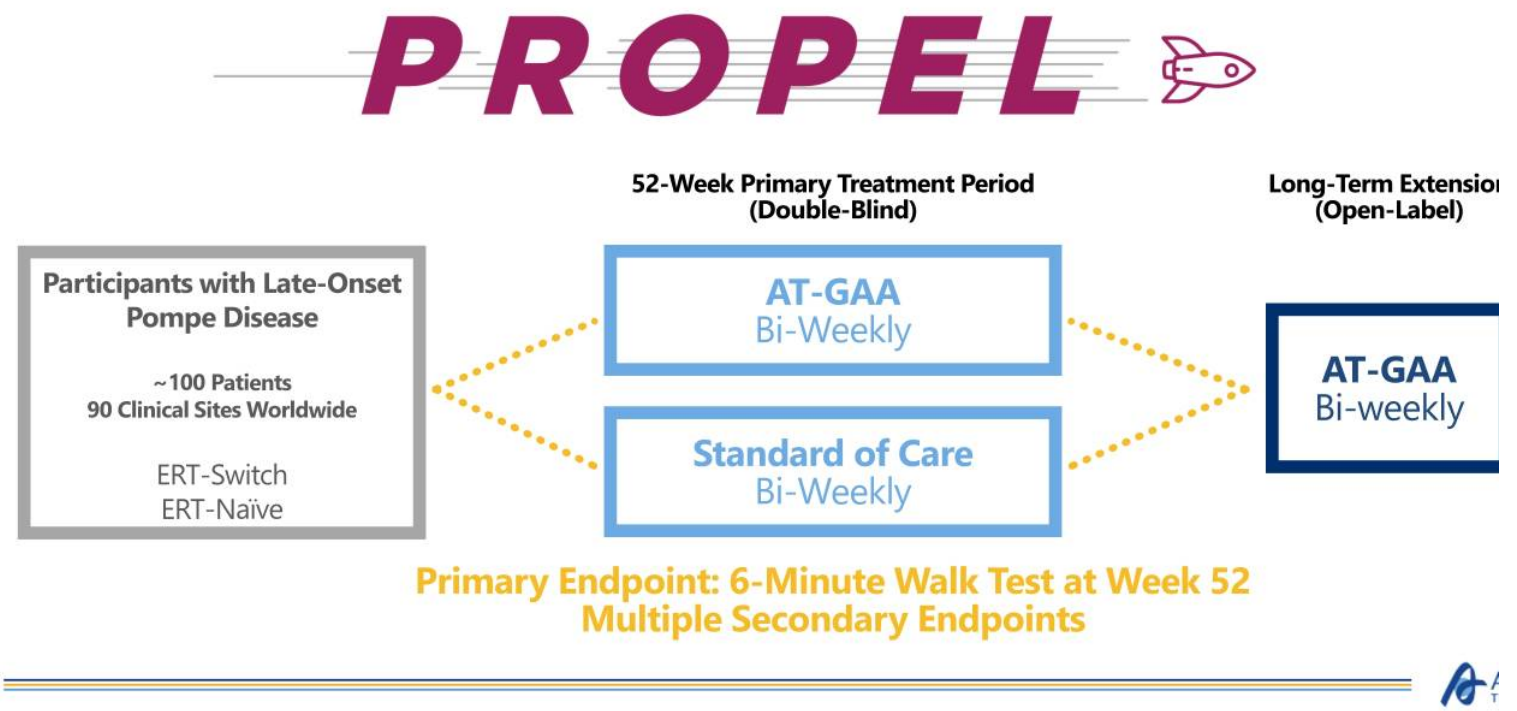
AT-GAA BTD Based on Ph 1/2 Clinical Efficacy

- Improvements in 6-minute walk distance
- Comparison to natural history of treated patients

BTD Features

- Intensive guidance on an efficient drug development program
- Organizational commitment involving senior managers
- All Fast Track program features
- Potential Rolling BLA
- Potential for Priority Review

PROPEL (ATB200-03) Study Design



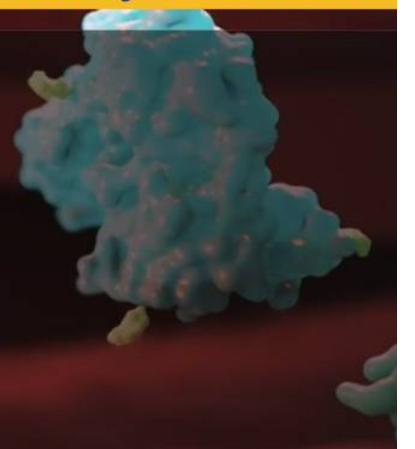
Pompe Biologics Manufacturing

Successful Scale Up to 1000L GMP Clinical and Commercial Scale to Fully Supply Global Pompe Population

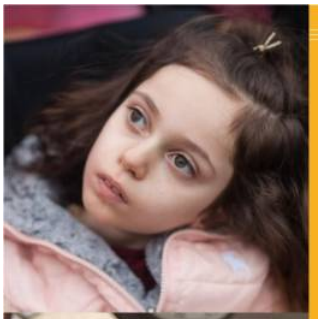
- Key quality attributes maintained from 5L to 250L to 1000L
- Agreements on biocomparability with key regulators (FDA, BfARM)
- PROPEL participants now treated with drug manufactured at 1000L
- Current bioreactor capacity to supply global population
- WuXi partnership strengthened with 5-year supply agreement

AT-GAA: 2019 Objectives

Advance AT-GAA for as Many Patients Worldwide as Quickly as Possible



- ✓ **Additional Phase 1/2 Data (up to 24 Months)**
- ✓ **Breakthrough Therapy Designation**
- ✓ **Full enrollment of Phase 1/2 Study (Cohorts 1-4)**
- • **Full enrollment of PROPEL study (n=100)**
- • **Present additional Phase 1/2 data (Cohort 4)**
- • **Report natural history study data**
- • **Initiate supportive pediatric study**
- • **Advance agreed upon CMC requirements to support BLA**



Gene Therapy Pipeline

"We have a duty to obsolete our own technologies

- Amicus Belief Statemer

Leading Lysosomal Disorder Gene Therapy Portfolio

Multiple Platforms Provide 14 Gene Therapy Programs and R&D Engine for Future Gro

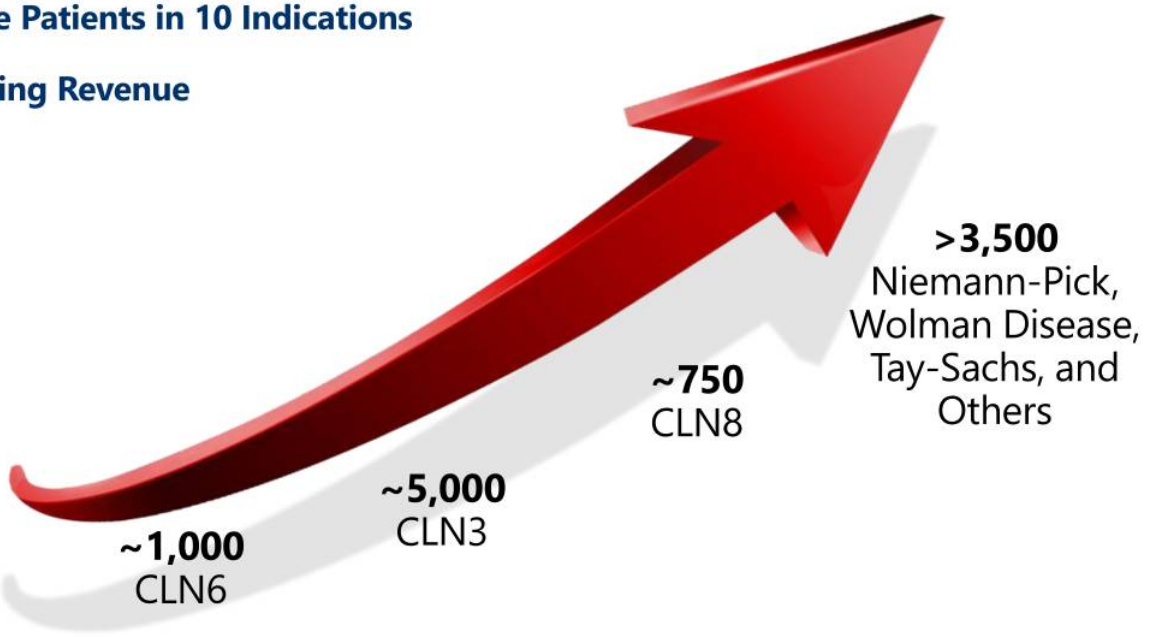
Gene Therapy Program Updates

- Positive initial preclinical data for Pompe gene therapy
- CLN3 Batten Disease Phase 1/2 Study Enrolling; Low Dose Cohort Complete (n=3)
- Additional 2-Year CLN6 Batten Disease Phase 1/2 Data on Track for 3Q19
- Additional preclinical studies in progress including CLN8, CLN1, Pompe and Fabry
- R&D Engines for Future Growth

Addressable Patient Populations in Neurologic LSDs*

10,000+ Addressable Patients in 10 Indications

$1B+ Annual Recurring Revenue

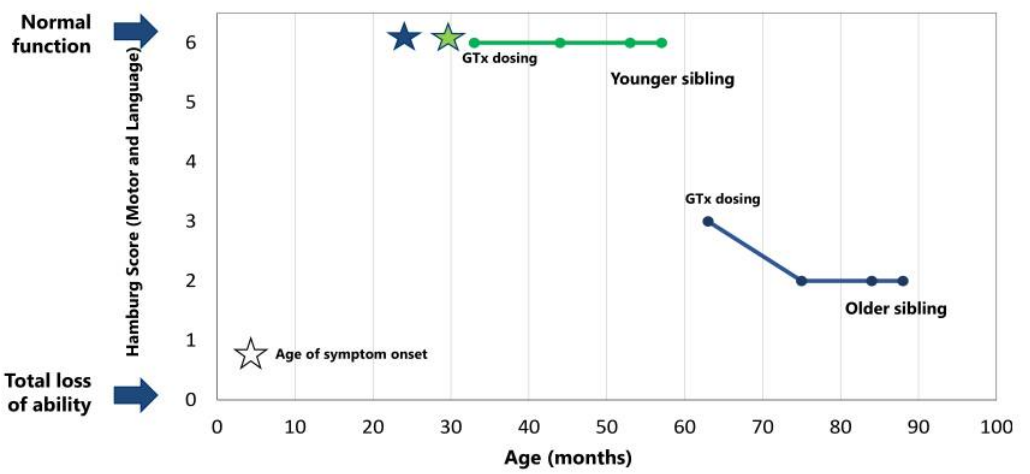


NATIONWIDE CHILDREN'S

*Estimated addressable U.S., EU, Japan, and other major, reimbursable markets based on published incidence and prevalence

Efficacy Data: Matched Sibling Case Report

Encouraging Interim Efficacy Data in First Two Patients Treated with Gene Thera with Two Years of Follow-up

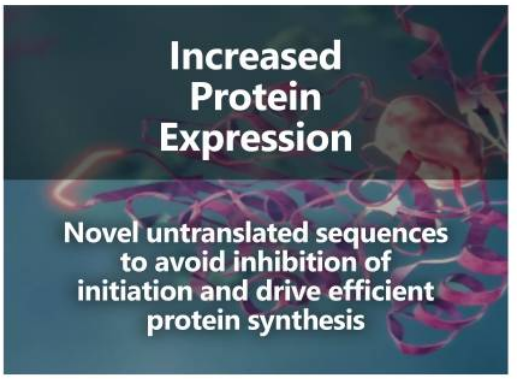


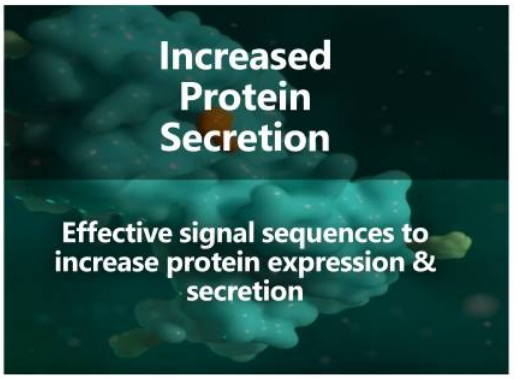
- Two siblings (same genotype) treated with gene therapy at a 2.8 and 5.3 years, respectively
- Two years post treatment, Hamburg motor and languag scores indicate no disease progression in the younger sibling
- Disease progression in older sibling has shown evidence of stabilization

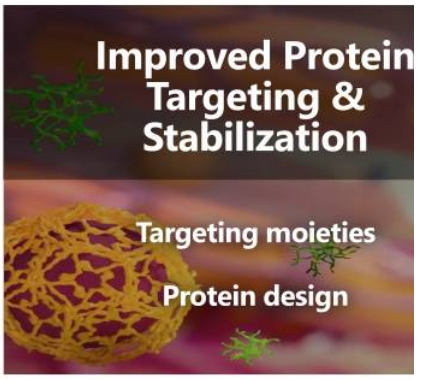
Source: Data on file

Amicus Protein Engineering Expertise & Technologies for Gene Therap

Collaboration to Enable Greater Protein Expression and Delivery at Lower Gene Therapy Dos







GENE THERAPY PROGRAM

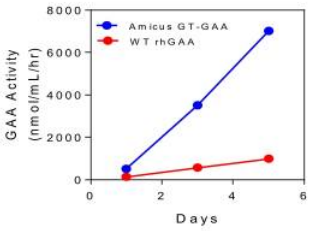
Penn

Early Proof of Principle for Optimized Gene Therapy

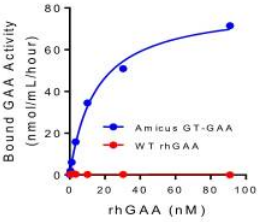
Amicus DNA Constructs Enable Optimized Gene Therapy in Pompe and Fabry

Pompe

Secreted GAA in Media

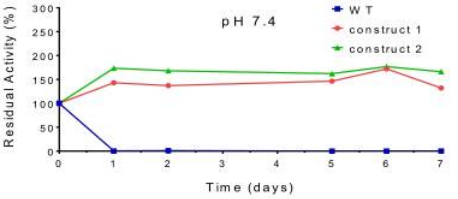


GAA Binding to Intended Receptor

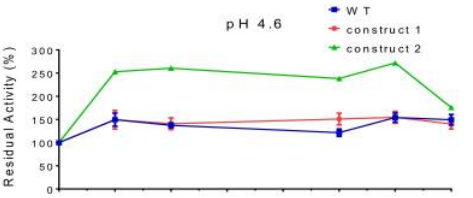


Fabry

Alpha-Gal Activity: pH 7.4



Alpha-Gal Activity: pH 4.6

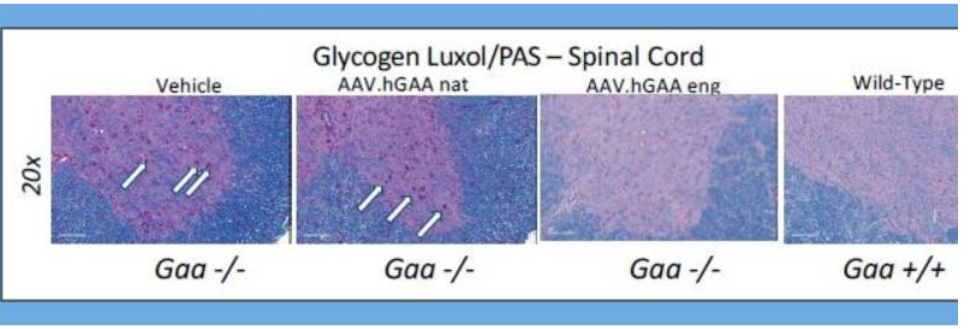


Preclinical Pompe Gene Therapy Results Presented at ASGCT

Initial Findings Validate Amicus/Penn Collaboration Combining Amicus-Engineered Transgenes with Penn's AAV G Therapy Technologies

Key findings:

- Improved cellular uptake and glycogen reduction observed with engineered AAV-hGAA
- Robust glycogen reduction in CNS observed only with engineered AAV-hGAA



Program Status and Anticipated Milestones

- Builds upon protein engineering and manufacturing expertise used to successfully dev AT-GAA
- Additional preclinical studies underway (various doses and routes of AAV administratio
- Selection of clinical candidate in 2019 to move into IND-enabling studies
- Platform potential to design constructs that enhance protein targeting across multiple lysosomal disorders

Manufacturing: Three-Pronged Approach

Proven Amicus Track Record in Biologics Manufacturing Applies to Gene Therapy

Now

GMP clinical supply available for ongoing studies at NCH

Validated vector engineering and manufacturing at UPenn

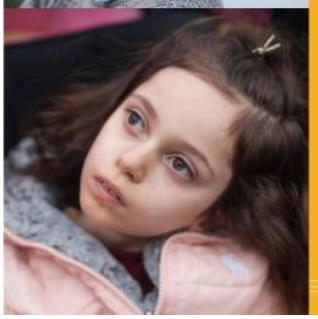
Mid Term

NCH and UPenn to supply initial clinical studies

Finalize partners for contract manufacturing

Long Term

Amicus manufacturing



Financial Summary & Milestones

"We have a duty to obsolete our own technologies
- Amicus Belief Statemer

Financial Summary and Guidance

Strong Balance Sheet with $435M+ Cash at 3/31/19- Cash Runway into 2021

FINANCIAL POSITION	March 31, 2019
Cash	~$438M
Cash Runway	Into at least mid-2021
CAPITALIZATION	
Shares Outstanding	230,180,714
FINANCIAL GUIDANCE	
Projected YE 2019 Cash Balance	~$300M
Galafold Revenue Guidance	$160M-$180M

Anticipated Milestones: 2019

Well-Positioned to Create Significant Value for Patients and Shareholders in 201

Galafold: Fabry Disease

- FY19 revenue guidance $160M-$180M
- Growth in existing markets
- Expansion into new markets
- Diagnostic initiatives

AT-GAA: Pompe Disease

- ✓ Additional Phase 1/2 data (21 and 24 months)
- ✓ Breakthrough therapy designation (BTD) in LOPD
- ✓ Phase 1/2 study fully enrolled (Cohorts 1-4)
- PROPEL pivotal study enrollment (n=100)
- Additional Phase 1/2 data (Cohort 4)
- Natural history study data
- Additional supportive studies
- Advance CMC requirements to support BLA

Gene Therapy Program

- Ongoing CLN3 Batten disease Phase 1/2 study enrollment
- Additional 2-year data from C Batten disease Phase 1/2 stud
- Additional preclinical data including next-generation ge therapies for Fabry and Pomp
- Selection of Pompe AAV ge therapy clinical candidate to move into IND-enabling stu

Thank You

"Our passion for making a difference unites us"

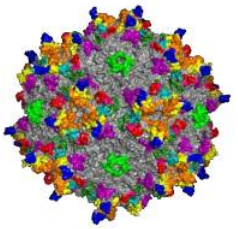
-Amicus Belief Statement

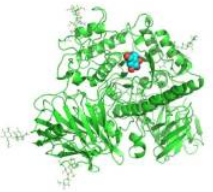
Amic
Therapeu

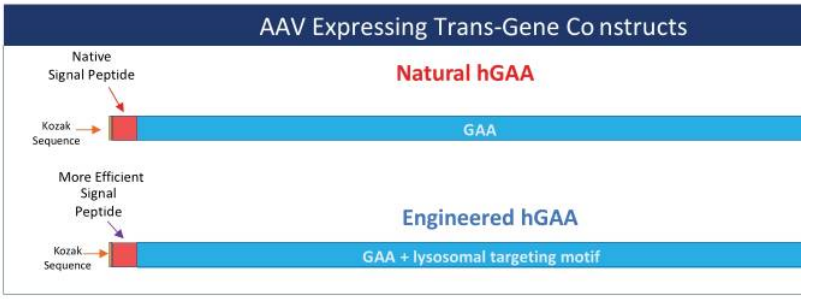
Appendix

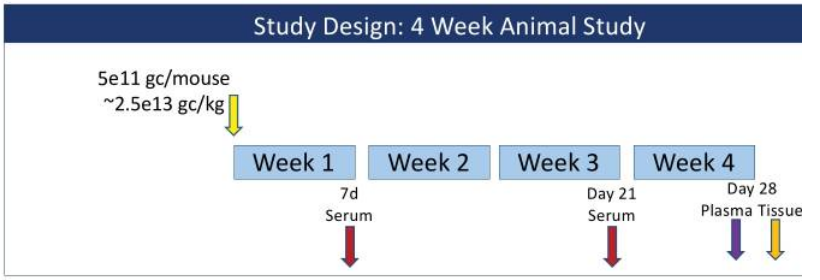
AAV Gene Therapy Initial High-Dose Preclinical POC Study

- AAV Transgene:
  - Natural-hGAA (AAV.hGAA nat)
  - Engineered-hGAA (AAV.hGAA eng)
- Dose\Route:
  - 5e11 gc/mouse (~2.5e13 gc/kg)
  - Tail Vein IV
- Animal Model:
  - Pompe Model *Gaa* -/- B6:129-GAAtm1Rabn/J (aka 6neo)
  - Wild-type *Gaa* +/+ (Pompe model litter-mates)
- Gender:
  - Male
  - Female
- Age: 4-6 weeks at AAV dosing



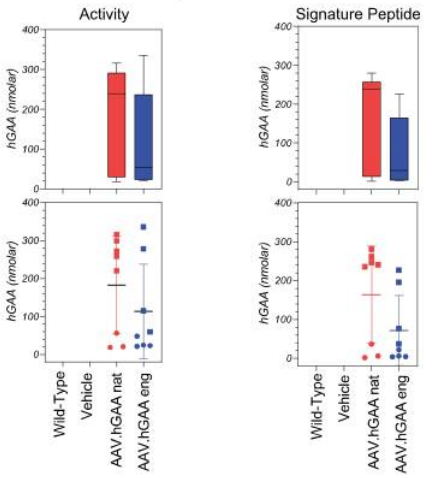






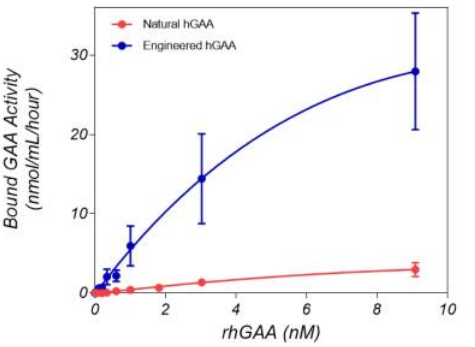
GAA Plasma Activity, Concentration and Cell-Surface Receptor Bindi

Day 28 Plasma



- High levels of engineered and natural hGAA were measured in plasma at day 28

Binding to Intended Receptor



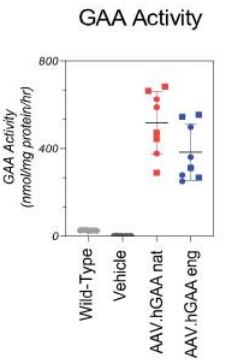
Day 28 Plasma Samples used to evaluate receptor binding

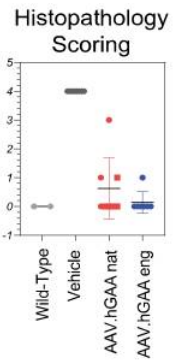
- Engineered hGAA was able to efficiently bind the intended receptor to enable cellular uptake

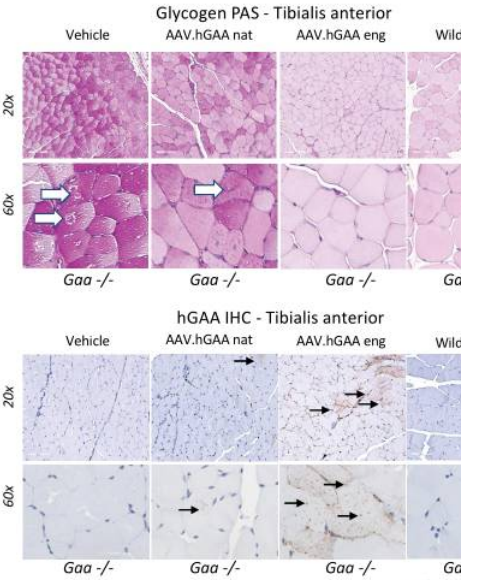
Tibialis Anterior – 28 days after AAV Gene Therapy

Engineered hGAA was more Efficient at Cross-Correction as Indicated by Greater Cellular Uptake, Uniform Glycogen Reduction ar Pathology Correction

- GAA activity in the tibialis anterior was ~15 – 20 fold higher than wild-type levels for both engineered hGAA and natural hGAA
- PAS staining showed more uniform and complete glycogen reduction and clearance of autophagic vacuoles for engineered hGAA
- PAS staining showed incomplete glycogen reduction and less clearance of autophagic vacuoles for natural hGAA (white arrows)
- IHC illustrated greater cellular uptake (black arrows) of engineered hGAA compared to natural hGAA
- Similar results seen in other muscle groups (see Appendix)





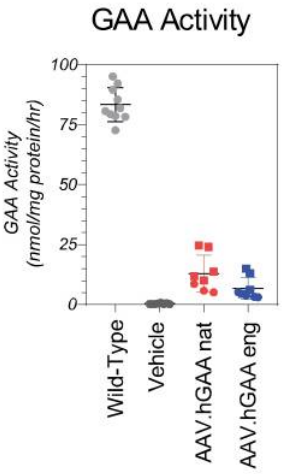


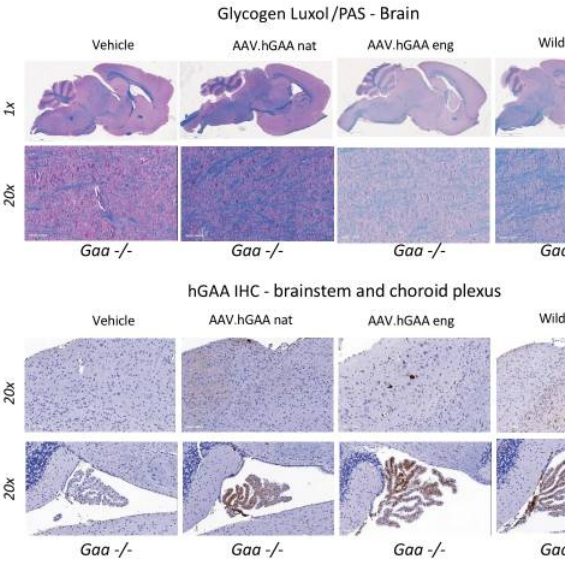
Periodic acid–Schiff (PAS) is a staining method used to detect polysaccharides such as glycogen in tissues

Brain– 28 days after AAV Gene Therapy

Engineered hGAA was able to Cross-Correct the Brain at Low Levels Due to Efficient Cellular Uptake while Natural hGAA was not a Cross-Correct at Similar Expression Levels

- GAA activity in the brain was ~5-fold lower than wild-type levels for both engineered hGAA and natural hGAA
- Both engineered hGAA and natural hGAA likely produced by the choroid plexus and secreted into the cerebrospinal fluid
- Glycogen close to wild-type levels for engineered hGAA, even though activity was only 20% of wild-type levels
- Little/no glycogen clearance with natural hGAA





Spinal Cord– 28 days after AAV Gene Therapy

Engineered hGAA was able to Reduce Glycogen Efficiently in the Spinal Cord while Little Glycogen Reduction was Observed for N hGAA

- PAS staining showed that glycogen levels were close to wild-type in ventral horn, including motor neurons, for engineered hGAA
- PAS staining showed that glycogen levels were closer to vehicle in ventral horn, including motor neurons, for natural hGAA (white arrows)
- IHC demonstrated a stronger signal in motor neurons from animals receiving engineered hGAA compared with natural hGAA (black arrows)