# 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): **October 11, 2018**

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

| | | |
|---|---|---|
| **Delaware** | | |
| (State or Other Jurisdiction of Incorporation) | | |
| **001-33497** | | **71-0869350** |
| (Commission File Number) | | (IRS Employer Identification No.) |
| **1 Cedar Brook Drive, Cranbury, NJ** | | **08512** |
| (Address of Principal Executive Offices) | | (Zip Code) |

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))

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

**Item 8.01. Other Events**

On October 11, 2018, Amicus Therapeutics, Inc. issued a press release announcing it will be hosting an Analyst Day on October 11, 2018 in New York City. A copy of the press release is attached to this Current Report on Form 8-K as Exhibit 99.1 and a copy of the presentation materials are attached hereto as Exhibit 99.2. Both exhibits are incorporated herein by reference.

**Item 9.01. Financial Statements and Exhibits.**

**(d) Exhibits:**

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release dated October 11, 2018. |
| 99.2 | October 11, 2018 Presentation Materials. |



**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.

Date: October 11, 2018

By: /s/ Ellen S. Rosenberg
Name: Ellen S. Rosenberg
Title: General Counsel and Corporate Secretary

**Amicus Therapeutics to Host Analyst Day 2018**
**Today in New York City**

Management and External Thought Leaders to Highlight
Robust Portfolio of Novel Therapies for Rare Metabolic Diseases

Webcast Scheduled from 8:30am — 12:30pm E.T.

**CRANBURY, NJ, October 11, 2018 -** Amicus Therapeutics, Inc. (NASDAQ: FOLD), a global biotechnology company focused on discovering, developing and delivering novel medicines for rare metabolic diseases will host its Analyst Day today, October 11, 2018, in New York City from 8:30 a.m. until 12:30 p.m. Eastern Time.

John F. Crowley, Chairman and Chief Executive Officer of Amicus Therapeutics, Inc., stated, "We are most pleased today to host our Analyst Day to highlight the depth and breadth of our leading portfolio of medicines for rare metabolic diseases. With one globally approved medicine for Fabry disease, a differentiated biologic for Pompe disease in the clinic and the recent addition of fourteen new gene therapy programs into our pipeline, including two clinical stage gene therapies for Batten disease, we are in a stronger position than ever to become a leading global biotechnology focused on transforming the lives of people living with these rare, life-threatening conditions."

**Amicus Analyst Day Featured Discussion Topics:**

- **Vision, Mission and Strategy**
  - John F. Crowley - Chairman and CEO, Amicus Therapeutics
- **Proof-of-Concept Data for AAV Gene Therapy Programs for Neurologic Lysosomal Storage Disorders**
  - Kathrin Meyer, Ph.D. — Principal Investigator, Nationwide Children's Hospital Center for Gene Therapy
  - Jay Barth, M.D. — Chief Medical Officer, Amicus Therapeutics
- **New Platforms for Gene Therapy in Rare Metabolic Disorders**
  - Jeff Castelli, Ph.D. — Chief Portfolio Officer, Amicus Therapeutics
  - James M. Wilson, M.D., Ph.D. — Professor of Medicine and Pediatrics, Perelman School of Medicine
  - Hung Do, Ph.D. — Chief Science Officer, Amicus Therapeutics
- **AT-GAA Positive 18-Month Data from Phase 1/2 Study (ATB200-02) for Pompe Disease**
  - Mark Roberts, M.D. - Dept. of Neurology, Salford Royal NHS Foundation Trust
- **Patient Advocacy and Personal Perspectives on Pompe Disease:**
  - Jayne Gershkowitz - Chief Patient Advocate, Amicus Therapeutics
  - George Fox - Dad and caregiver to son, Phoenix
  - Mike Stanzione — courageously living with late onset Pompe
- **Galafold Global Launch Updates**
  - Bradley Campbell — President and COO, Amicus Therapeutics
  - Detlef Wolff — SVP, Head of International, Amicus Therapeutics

The live event will be audio webcasted simultaneously and accessible through the Events & Presentations page of the Amicus Therapeutics website at http://ir.amicusrx.com/. The event will be archived on the Company's website for approximately 90 days.

**About Amicus Therapeutics**

Amicus Therapeutics (Nasdaq: FOLD) is a global, patient-centric biotechnology company focused on discovering, developing and delivering novel high-quality medicines for people living with rare metabolic diseases. With extraordinary patient focus, Amicus Therapeutics is committed to advancing and expanding a robust pipeline of cutting-edge, first- or best-in-class medicines for rare metabolic diseases. For more information please visit the company's website at www.amicusrx.com.

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**Forward Looking Statement**

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to the collaboration with the University of Pennsylvania, the recent acquisition of Celenex, preclinical and clinical data, regulatory strategy and the development of potential gene therapy product candidates. The inclusion of forward-looking statements should not be regarded 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 out to be wrong and can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. For example, the benefits of this collaboration may never be realized, the potential that results of clinical or preclinical studies indicate that the product candidates are unsafe or ineffective; the potential that it may be difficult to enroll patients in our clinical trials; the potential that regulatory authorities, including the FDA, EMA, and PMDA, may not grant or may delay approval for our product candidates; the potential that preclinical and clinical studies could be delayed because we identify serious side effects or other safety issues; the potential that we may not be able to manufacture or supply sufficient clinical or commercial products; the potential that we will need additional funding to complete all of our studies and manufacturing and the potential that certain individuals may not continue to support the development of product candidates. . In addition, all forward-looking statements are subject to other risks detailed in our Annual Report on Form 10-K for the year ended December 31, 2017 as well as our Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 filed August 7, 2018 with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, and we undertake no obligation to revise or update this presentation to reflect events or circumstances after the date hereof.

CONTACTS:

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(609) 662-5044

**Media / Multimedia Assets:**
Pure Communications
Jennifer Paganelli
jpaganelli@purecommunications.com
(347) 658-8290

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Amicus Therapeutics®

# Amicus 2018 Analyst Day

**October 11, 2018 | New York, NY**



## Forward Looking Statements

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# Agenda

| | | |
|---|---|---|
| 8:30 a.m. – 8:35 a.m. | WELCOME & INTRODUCTIONS | Sara Pellegrino, *Vice President, Investor Relations and Corporate Comm* |
| 8:35 a.m. – 8:50 a.m. | VISION, MISSION AND STRATEGY | John F. Crowley, *Chairman and Chief Executive Officer* |
| 8:50 a.m. – 9:50 a.m. | AAV GENE THERAPY PLATFORM FOR NEUROLOGIC LSDs | **Strategic Fit for Amicus Entry into Gene Therapy**<br>John F. Crowley, *Chairman and Chief Executive Officer* |
| | | **AAV Platform Overview and Proof of Concept Data**<br>Kathrin Meyer, Ph.D., *Principal Investigator, Nationwide Children's Hosp* |
| | | **CLN6 Clinical Summary**<br>Jay Barth, M.D., Chief Medical Officer |
| | | **Q&A and Break** |
| 10:00 a.m. – 10:30 a.m. | NEW PLATFORMS FOR GENE THERAPY IN RARE METABOLIC DISORDERS | **Amicus-UPenn Collaboration and Perspectives on Gene Therapy Appr**<br>James M. Wilson, M.D., Ph.D., *Professor of Medicine and Pediatrics at t* |
| | | **Applying Amicus Expertise to Optimize Gene Therapy**<br>Hung Do, Ph.D., *Chief Science Officer* |
| | | **Q&A** |
| 10:30 a.m. – 11:40 a.m. | AT-GAA – POTENTIAL TO SHIFT TREATMENT PARADIGM FOR POMPE DISEASE | **AT-GAA Phase 1/2 18-Month Data**<br>Mark Roberts, M.D., *Dept. of Neurology, Salford Royal NHS Foundation* |
| | | **Patient Advocacy and Personal Perspectives on Pompe Disease**<br>• Jayne Gershkowitz, *Chief Patient Advocate*<br>• George Fox, *Dad and Caregiver to son, Phoenix*<br>• Mike Stanzione, *Courageously living with late-onset Pompe* |
| | | **AT-GAA Development Strategy**<br>John F. Crowley, *Chairman and Chief Executive Officer* |
| 11:40 a.m. – 12:00 p.m. | GALAFOLD ORAL PRECISION MEDICINE FOR FABRY DISEASE | **Global Launch Overview**<br>Bradley Campbell, *President and Chief Operating Officer*<br>Detlef Wolff, *Senior Vice President, Head of International* |
| 12:00 p.m. – 12:10 p.m. | CLOSING REMARKS | John F. Crowley, *Chairman and Chief Executive Officer* |
| 12:10 p.m. – 12:30 p.m. | Q&A SESSION | |

# Vision, Mission & Strategy

**John F. Crowley**

*2018 Analyst Day | October 11, 2018 | Ne*

# Amicus Today

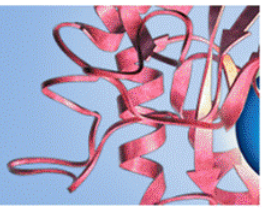
Galafold™ (migalastat)

First Oral Precision Medicine for Fabry Disease

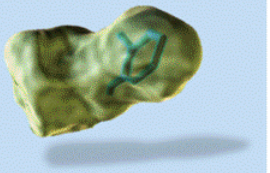
**500+ EMPLOYEES globally**

**PIP**
of 13 p
metal

**BIOLOGICS PLATFORM**
Protein Engineering & Glycobiology

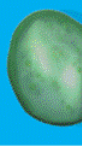


**AT-GAA***
Investigational Therapy for Pompe in Phase 3



**GLOBAL FOOTPRINT**
in 27 countries

Leading
Lysos
Stora
Disor



approx. **$550M** Cash (6/30/18)

**Gene Therapy Platforms**

* AT-GAA, also known as ATB200/AT2221



# Robust Rare Disease Portfolio

| | DISCOVERY | PRECLINICAL | PHASE 1/2 | PHASE 3 | REGULATORY |
|---|---|---|---|---|---|
| **Fabry Franchise** | | | | | |
| Galafold™ (Migalastat) monotherapy | | | | | |
| Fabry Gene Therapy | UPENN | | | | |
| **Pompe Franchise** | | | | | |
| AT-GAA (Novel ERT + Chaperone) | | | | | |
| Pompe Gene Therapy | UPENN | | | | |
| **Other Gene Therapy Programs** | | | | | |
| CLN6 Batten Disease | NCH | | | | |
| CLN3 Batten Disease | NCH | | | | |
| CLN8 Batten Disease | NCH | | | | |
| Neimann Pick C | NCH | | | | |
| Wolman Disease | NCH | | | | |
| Tay Sachs | NCH | | | | |
| Multiple Other CNS LSDs | NCH | | | | |
| CDKL5 Gene Therapy / ERT | UPENN | | | | |
| Other | UPENN | | | | |

Advancing One o
Robust Portfolio
Diseases in
Biotechnol

# 2018 Key Strategic Priorities

**On Track to Achieve All FIVE Key Strategic 2018 Priorities Outlined in Janu**

1. **Double Galafold (migalastat) revenue to $80-$90M**
2. ✓ **Secure approvals for migalastat in Japan and the U.S.**
3. ✓ **Achieve clinical, manufacturing and regulatory milestones to advance AT-GAA toward global regulatory submissions and approvals**
4. ✓ **Develop and expand preclinical pipeline to ensure at least one new clinical program in 2019**
5. ✓ **Maintain financial strength**



# What's New at Amicus Analyst Day

**10 Important New Data Points and Updates to Share Today**

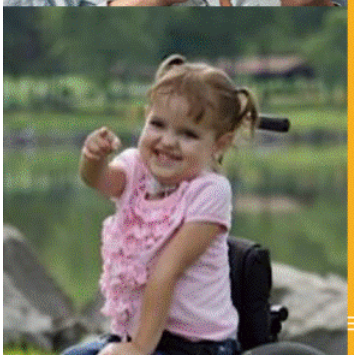
- Clinical safety data for lead CLN6 Batten disease program
- Additional proof of concept for CLN8 Batten Program
- Preliminary Amicus DNA constructs for Pompe Gene Therapy
- Preliminary Amicus DNA constructs for Fabry Gene Therapy
- Amicus/Penn AAV gene therapy approach and strategies
- AT-GAA patient-level data on 6-minute walk test at 18 months
- AT-GAA muscle strength data at 18 months
- Galafold milestone of 500 patients reached in Q3 for Internatio
- Current International market dynamics and trends
- Galafold U.S. adoption trends and key metric 8 weeks into laun

# Key Takeaways for Amicus Analyst Day

- **Vision 2023: 5,000+ Patients & $1B+ in Revenue**
- **Galafold: Cornerstone of Success**
  - $500M+ Peak Revenue Potential
  - $1B+ Cumulative Revenue from 2019E-2023E to Drive R&D Engine
- **AT-GAA: The Crown Jewel**
  - Highly differentiated ERT with Potential to Obsolete Current Standard of Care
  - $1B+ Peak Revenue Potential
- **Gene Therapy: Foundation for the Future**
  - Amicus as "Best in Class" Consolidator and Integrator
  - Potential $1B+ in Recurring Peak Revenue from Current Gene Therapy Portfolio
- **World Class, Global Team of "Passionate Entrepreneurs "**
- **Extraordinary and Intense Patient Focus**

## Our Passion for Making a Difference Unites Us

# Rare Company Video



## Gene Therapy Pipeline in Rare Metabolic Diseases

John F. Crowley
Kathrin Meyer, Ph.D.
Jay Barth, M.D.
Jeff Castelli, Ph.D.

*2018 Analyst Day | October 11, 2018 | Ne*

# Amicus Establishes Gene Therapy Portfolio

**License Through Nationwide Children's Hospital Combines Successful Amicus Development and Commercial Track Rec**
**AAV Gene Therapy Programs for Rare Neurologic LSDs**

- Ground Breaking, Clinically Validated Science
- Ten Gene Therapy Programs
- Expertise and Relationships in Gene Therapy
- Compelling Data in Three Lead Programs
- Leading Gene Therapy Portfolio in Neurologic Lysosomal Storage Disorders

*"I firmly believe that Amicus*
*scientific and clinical partner*
*programs forward and I look*
*actively collaborating with th*
*on the development of these i*
*potential therapies."*

*- Kathrin Meyer, Ph.D. PI at M*
*Children's Hospital and Assistant*

Amicus AAV9 Gene Therapy Programs

# Validated Gene Therapy Platform

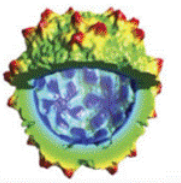
**Portfolio is Based on a Validated Gene Therapy Approach Across Multiple CNS**

## Clinically validated AAV gene therapy approach

- Nationwide Children's Hospital Center for Gene Therapy (NCH)
- Intrathecal delivery with robust expression throughout CNS

## Preclinical safety and efficacy studies replicated across multiple diseases at NCH

- SMA
- Rett Syndrome
- ALS
- CLN6
- CLN3



scAAV

**AAV9-CLN6 Transgene**


Foust, Kaspar et al, 2009

Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy

# Batten Disease Overview

## Batten Disease is a Group of Rare, Fatal, Lysosomal Storage Disorders of the Cent System with High Unmet Need and Limited Treatment Options

### Disease Overview

- A group of disorders known as neuronal ceroid lipofuscinoses (NCLs), collectively referred to as Batten disease
- Mutation in one of 13 different CLN genes leads to lysosomal dysfunction
- Signs and symptoms typically begin in early and late childhood
- Most affected children do not survive into adulthood

Source: Batten Disease Fact Sheet, NINDS, Publication date June 2018.

Amicus AAV9 Gene Therapy Programs

# Lead Program Status

## The CLN6 and CLN3 Program are Clinical Stage; CLN8 has Definitive Preclinical Effic Mouse Model of Disease

PRECLINICAL MOUSE MODEL DATA

| | Storage Material and Glial Activation | Motor & Cognitive Function | Survival | Safety & Brain Expression in NHP | GMP Clinical Supply | IND Active |
|---|---|---|---|---|---|---|
| **CLN6** | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **CLN3** | ✓ | ✓ | N/A* | ✓ | ✓ | ✓ |
| **CLN8** | ✓ | ✓ | ✓ | Pending | Pending | Pending |

*CLN3 mouse model does not have impaired survival

# Preclinical Proof of Concept Data in CLN6 Batten Disease

Kathrin Meyer, Ph.D.

## Disclosure Information

**I have the following financial relationships to disclose:**

- Consultant for Amicus Therapeutics, Inc.

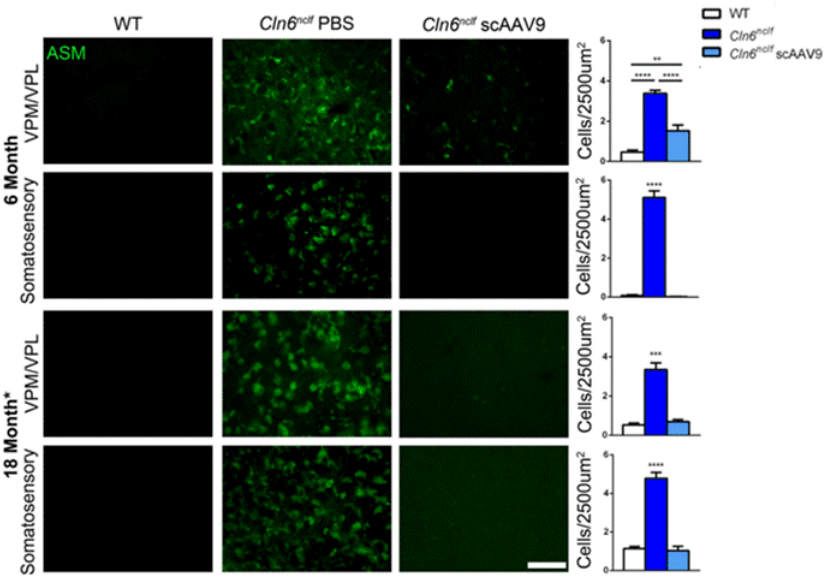
**I will discuss the following off-label use and/or investigational use in my presenta**

- Preclinical, proof of concept data from studies for the treatment of patients with Ba

# CLN6: Preclinical Mouse Data – Autofluorescent Storage Ma

## Single AAV9-CLN6 Administration Results in Reduction of Autofluorescent Substra Throughout the Brain

### Autofluorescent Storage Material Accumulation



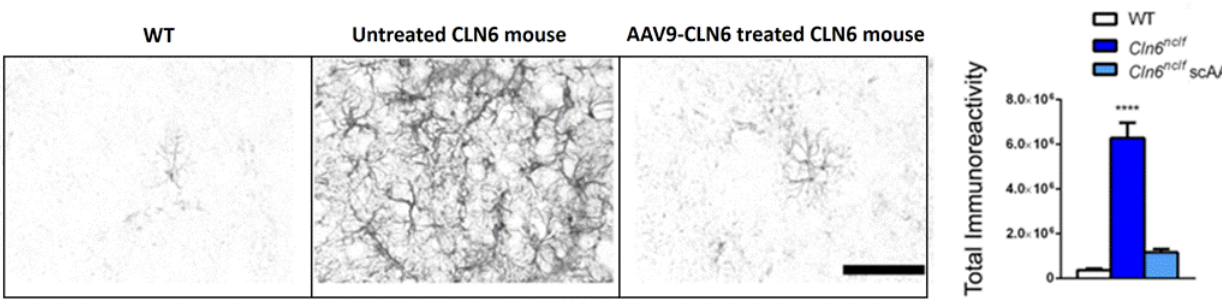

Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy

AAV9-CLN6 Gene Therapy for CLN6-Batten Disease

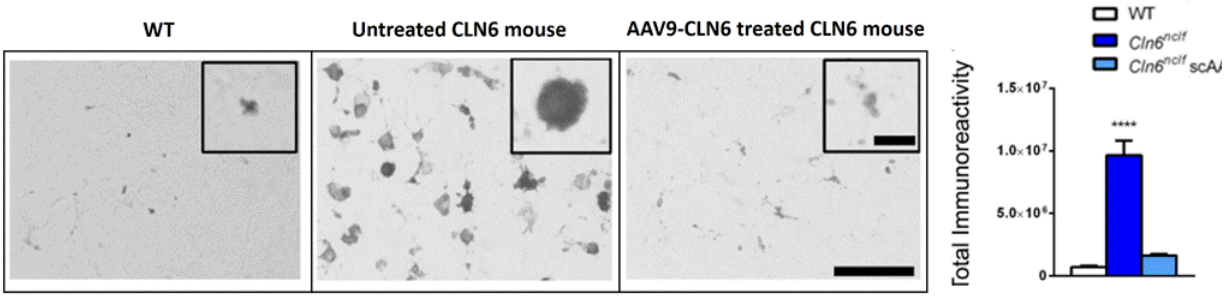
# CLN6: Preclinical Mouse Data – Somatosensory Glial Activat

## Single AAV9-CLN6 Administration Results in Reduction of Glial Activatio

**Astrocyte Activation: Month 18**




**Microglial Activation: Month 18**

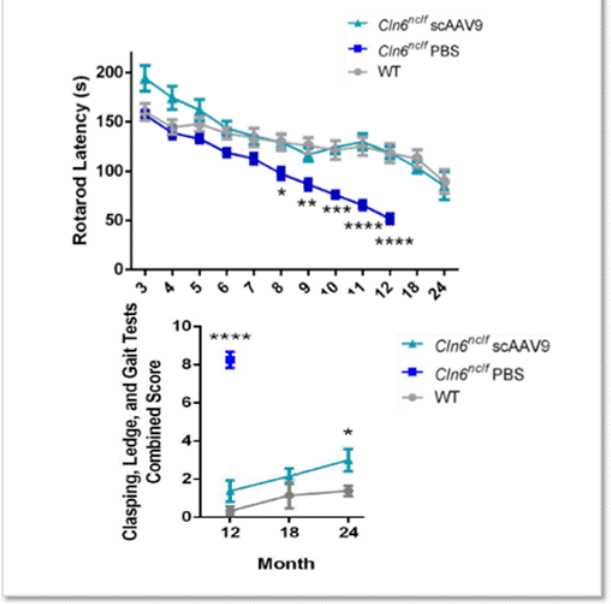


# CLN6: Preclinical Mouse Data

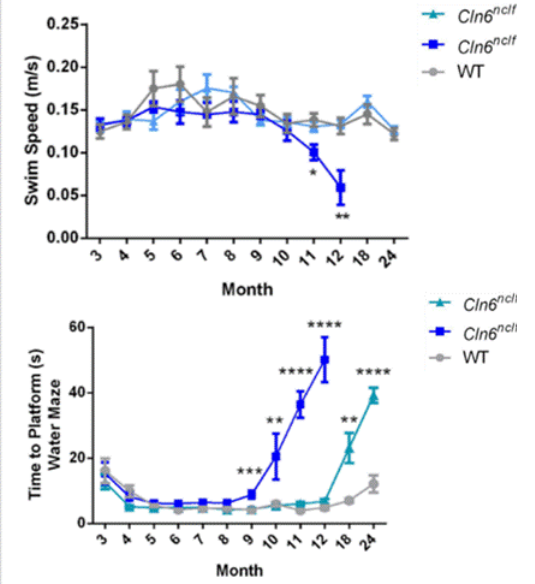
## Motor Performance and Cognitive Behavior

**Single AAV9-CLN6 Administration Improves Motor Performance & Cognitive Behavior Out to**

### Motor Performance




### Water Maze Analysis



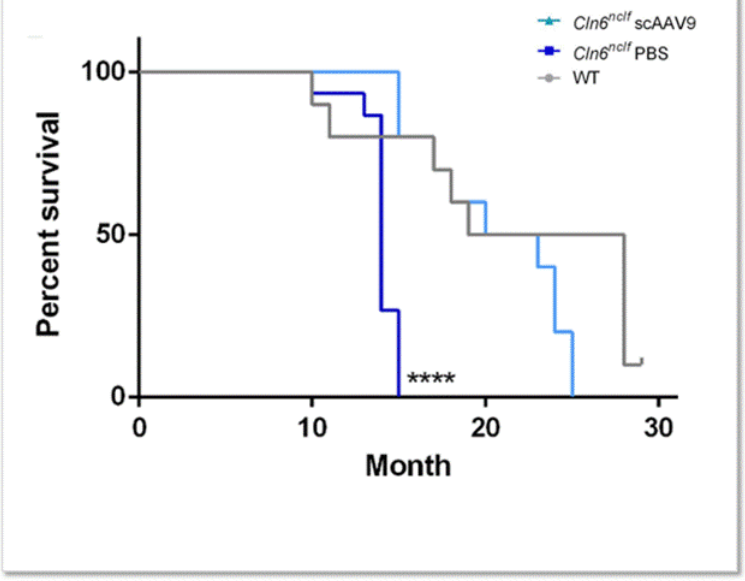

Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy; Data on file



# CLN6: Preclinical Mouse Data - Survival

**Single AAV9-CLN6 Administration Significantly Extends Median Survival**

### Survival

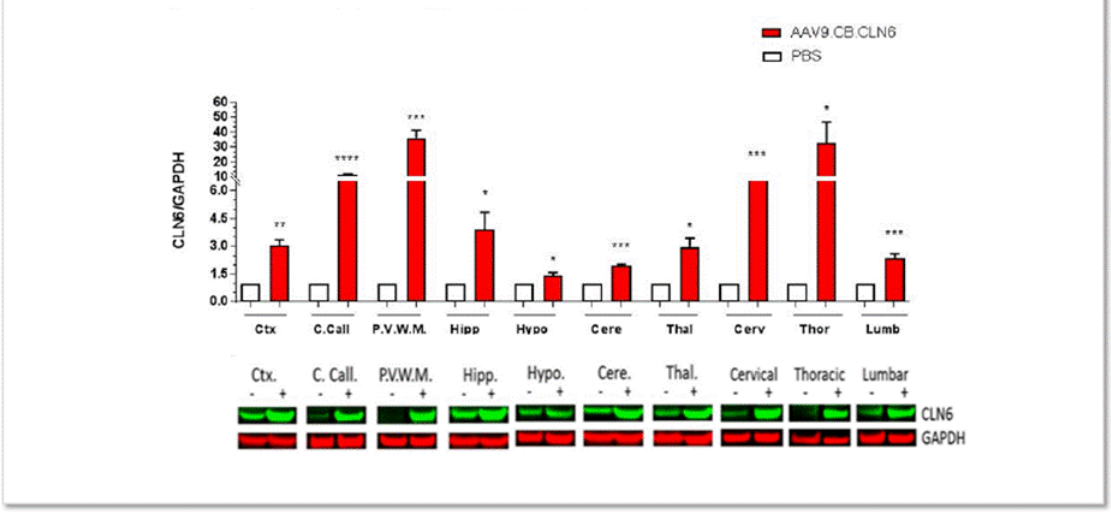



Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy

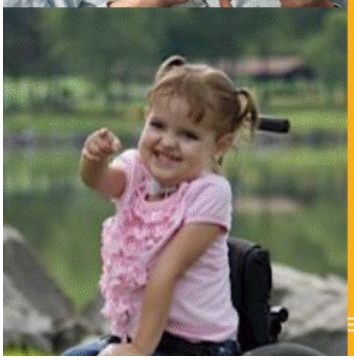
# CLN6 Expression in NHP Safety Study

## Demonstrated Safety and Meaningful Transduction and CLN6 Expression Throughout the Bra

**Western Blot on various brain regions of AAV9-CLN6 injected juvenile NHPs**




Source: Meyer 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, From mouse to human –Translating intrathecal gene therapy for NCLs; Data on file

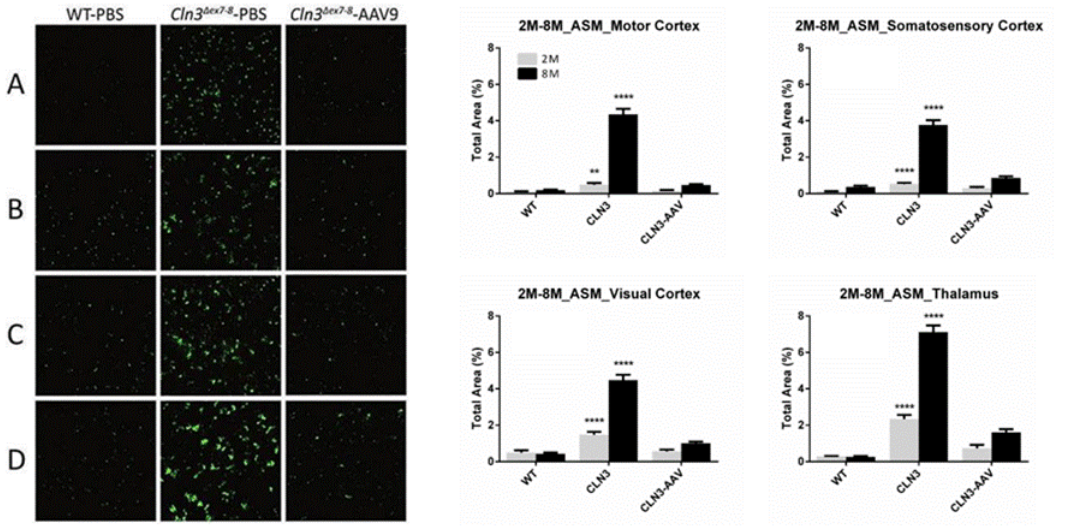


# Preclinical Proof of Concept Data in CLN3 Batten Disease

# CLN3: Preclinical Mouse Data – Autofluorescent Substrate I

## Single AAV9-CLN3 Administration Results in Reduction of Autofluorescent Substra Throughout the Brain

### Autofluorescent Storage Material Accumulation




Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy

AAV9-CLN3 Gene Therapy for CLN3-Batten Disease

# CLN3: Preclinical Mouse Data – Somatosensory Glial Activat

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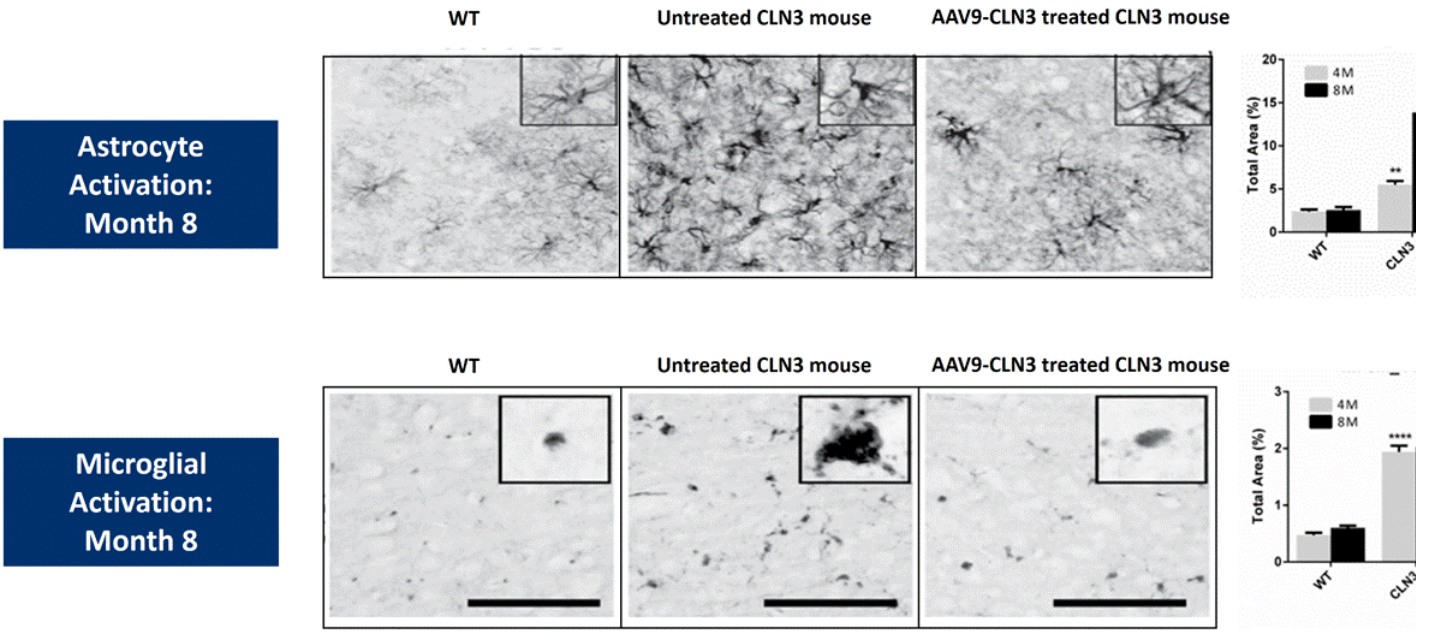
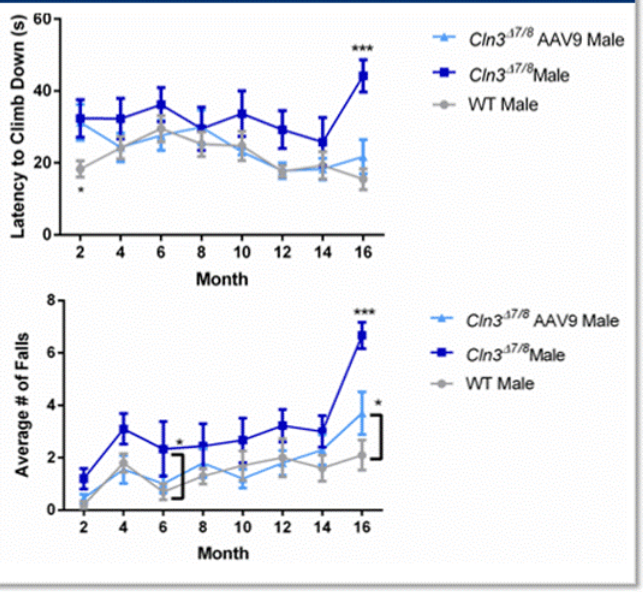



Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy

# CLN3: Preclinical Mouse Data - Motor Performance & Cognitive Be

## Single AAV9-CLN3 Administration Improves Motor Performance and Cognitive at Month 16

### Motor Performance

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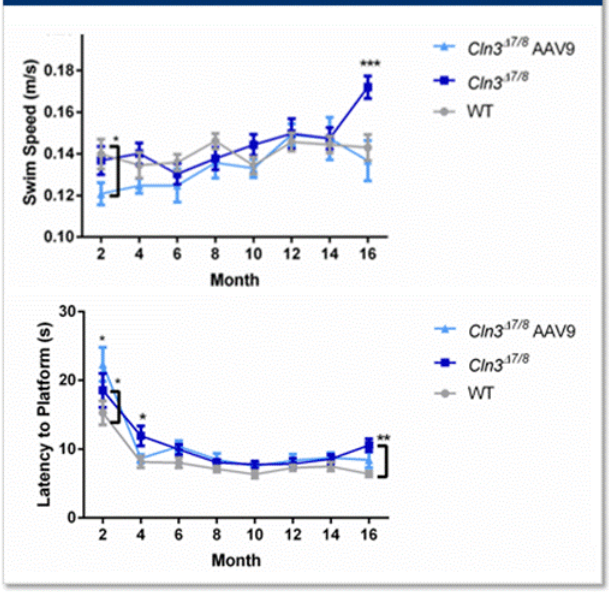


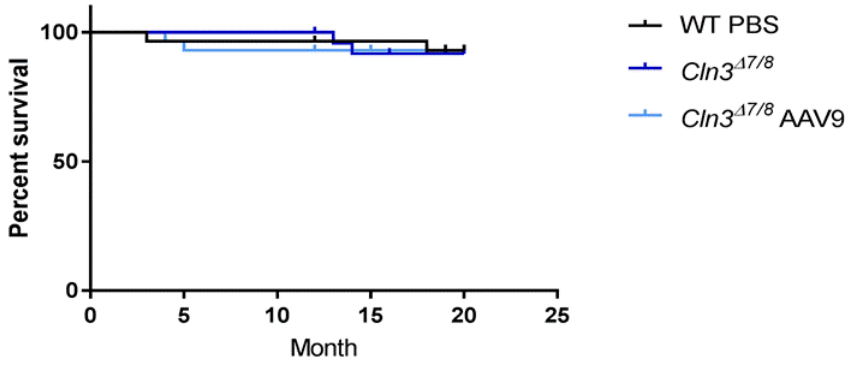

Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy



# CLN3: Preclinical Mouse Data - Survival

## Effect of AAV9-CLN3 On Survival Cannot Yet Be Determined Given Minimal Phenot Model

### Survival

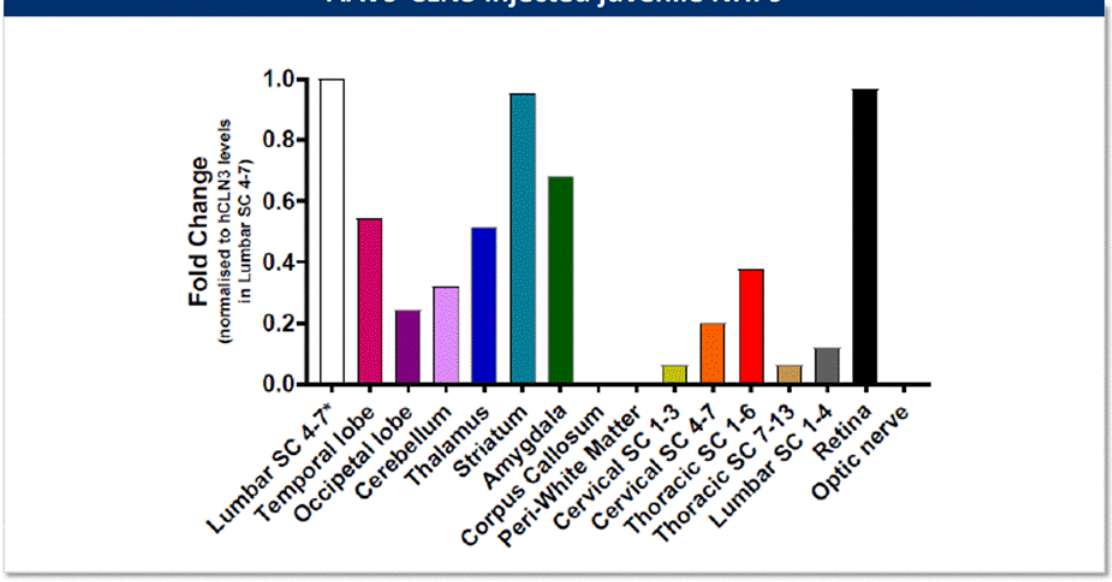



Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy

# CLN3 Expression in NHP Safety Study

## Demonstrated Safety and Meaningful Transduction and Expression Throughout the

**Reverse transcriptase qPCR on various brain regions of AAV9-CLN3 injected juvenile NHPs**




Note: CLN3 Western blot -data were not assessable

Source: Meyer 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, From mouse to human –Translating intrathecal gene therapy for NCLs;

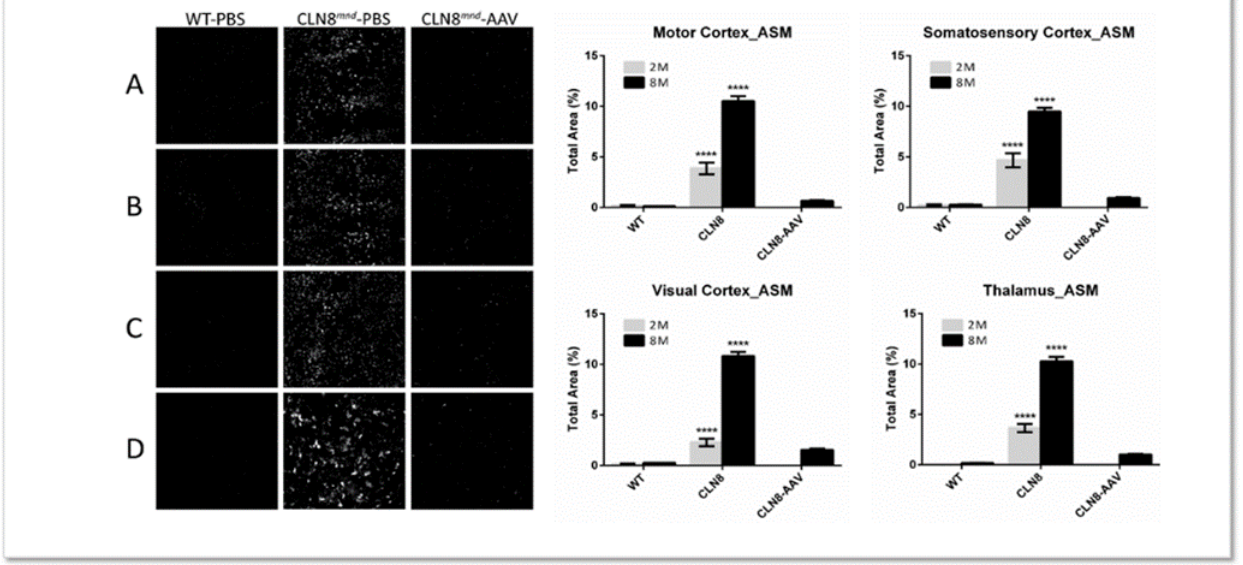
# Preclinical Proof of Concept Data in CLN8

## Program Overview

# CLN8: Preclinical Mouse Data – Autofluorscent Storage Mat

## Single AAV9-CLN8 Administration Results in Reduction of Autofluorescent Substra Throughout the Brain

### Autofluorescent Storage Material Accumulation



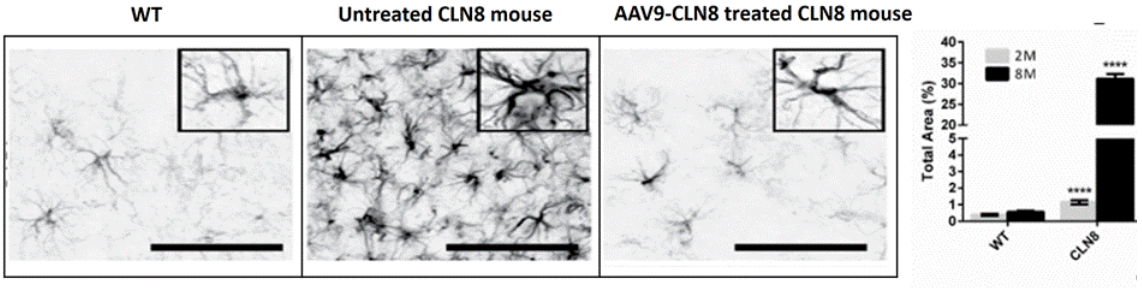

Source: Johnson 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, Testing the safety and efficacy of CLN8 gene therapy in the Cln8mnd mouse model



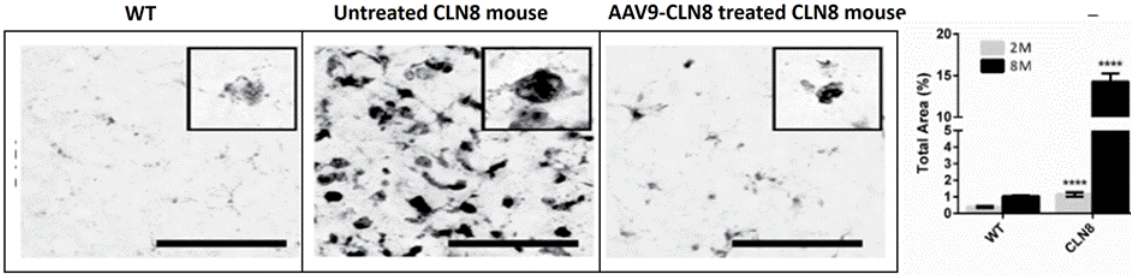
# CLN8: Preclinical Mouse Data - Somatosensory Glial Activati

## Single AAV9-CLN8 Administration Results in Reduction of Glial Activatio

**Astrocyte Activation: Month 8**




**Microglial Activation: Month 8**

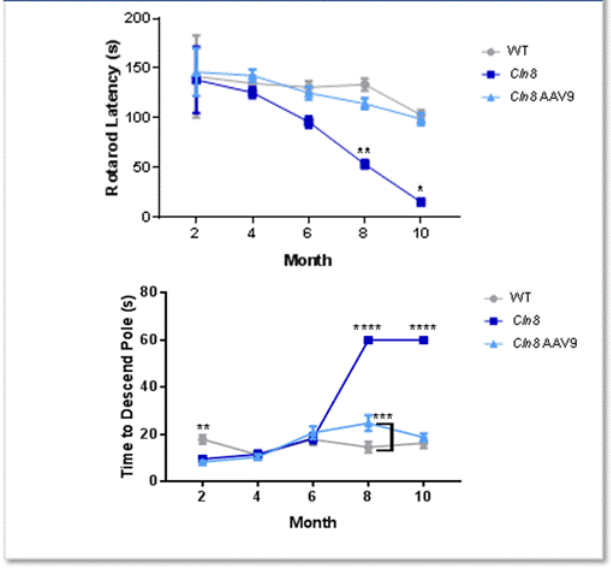



Source: Johnson 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, Testing the safety and efficacy of CLN8 gene therapy in the Cln8mnd mouse model

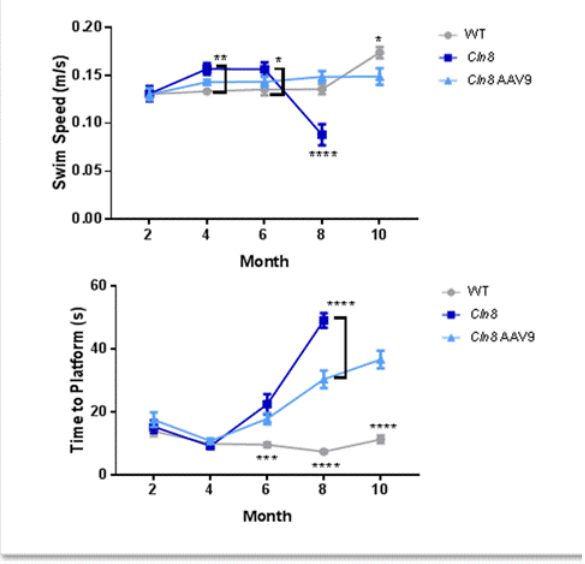
# CLN8: Preclinical Mouse Data - Motor Performance and Cognitive

## Single AAV9-CLN8 Administration Improves Motor Performance & Cognitive Behavior Out to Month 10

### Motor Performance




### Water Maze Analysis



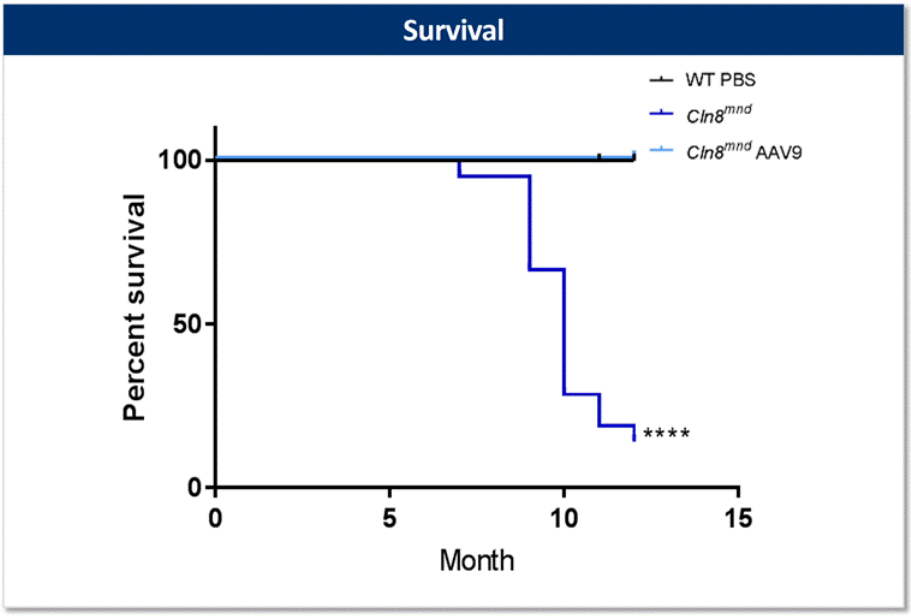

Source: Johnson 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, Testing the safety and efficacy of CLN8 gene therapy in the Cln8$^{mnd}$ mouse model

AAV9-CLN8 Gene Therapy for CLN8-Batten Disease

# CLN8: Preclinical Mouse Data - Survival

## Single AAV9-CLN8 Administration Significantly Extends Median Surviva

### Survival




Source: Johnson 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, Testing the safety and efficacy of CLN8 gene therapy in the Cln8$^{mnd}$ mouse model

# CLN6 Clinical Summary

**Jay Barth, M.D.**



## CLN6: Clinical Data Summary

**Encouraging Safety and Efficacy Data from an Ongoing Single-arm Phase 1/2**

- Single-arm study with all patients receiving gene therapy
  - Single intrathecal administration
- Ten patients currently treated; additional patients in screening
- Generally well-tolerated
- Encouraging preliminary efficacy data
- Additional data to be presented in 2019

# CLN6: Clinical Study Safety Summary Interim Data

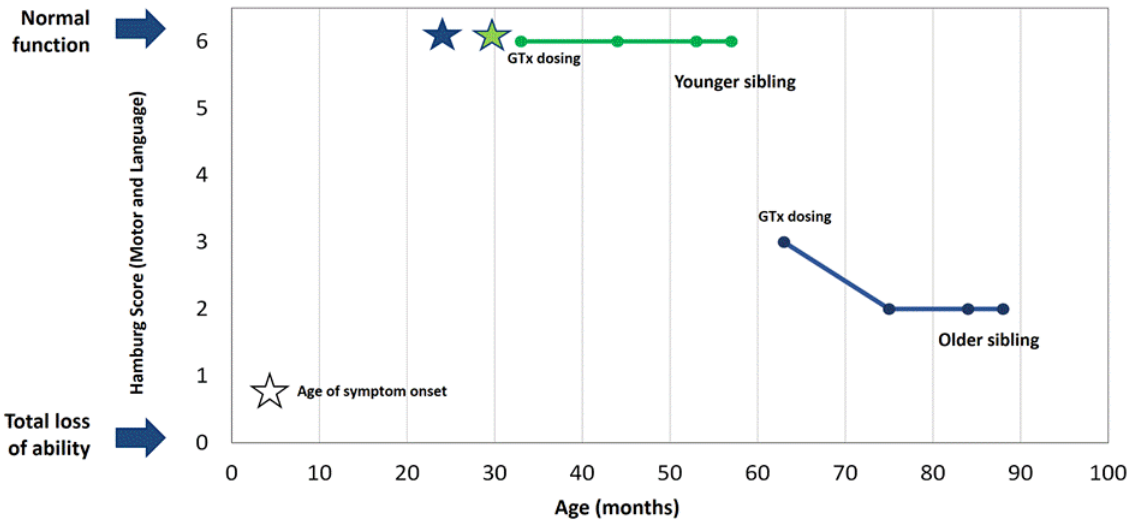
## Data from an Ongoing Single-arm Phase 1/2 Study Indicate Single AAV9-CLN6 Adm Generally Well Tolerated

- Ten patients currently treated with single intrathecal administration
  - Average follow-up duration: 12 months (range 1-24 months)
- Adverse events (n=94 events reported)
  - Majority of adverse events (AEs) were mild and unrelated to treatment
  - Five Grade 3 (severe) AEs (defined as medically significant) reported in 4 patients
  - No Grade 4 (life-threatening) or Grade 5 (death) AEs reported to date
- T-cell response and antibody elevations not associated clinical manifestations
  - No changes in treatment required
- Data Safety Monitoring Board (DSMB) has permitted study to proceed and enroll additional patie

AAV9-CLN6 Gene Therapy for CLN6-Batten Disease

# Efficacy Data: Matched Sibling Case Report

## Encouraging Interim Efficacy Data in First Two Patients Treated with Gene Therapy v of Follow-up




- Two siblings (same ge treated with gene the 2.8 and 5.3 years, res
- Two years post treatr motor and language s no disease progressio younger sibling
- Disease progression i has shown evidence

Source: Data on file

# Upcoming Batten Disease Program Milestones

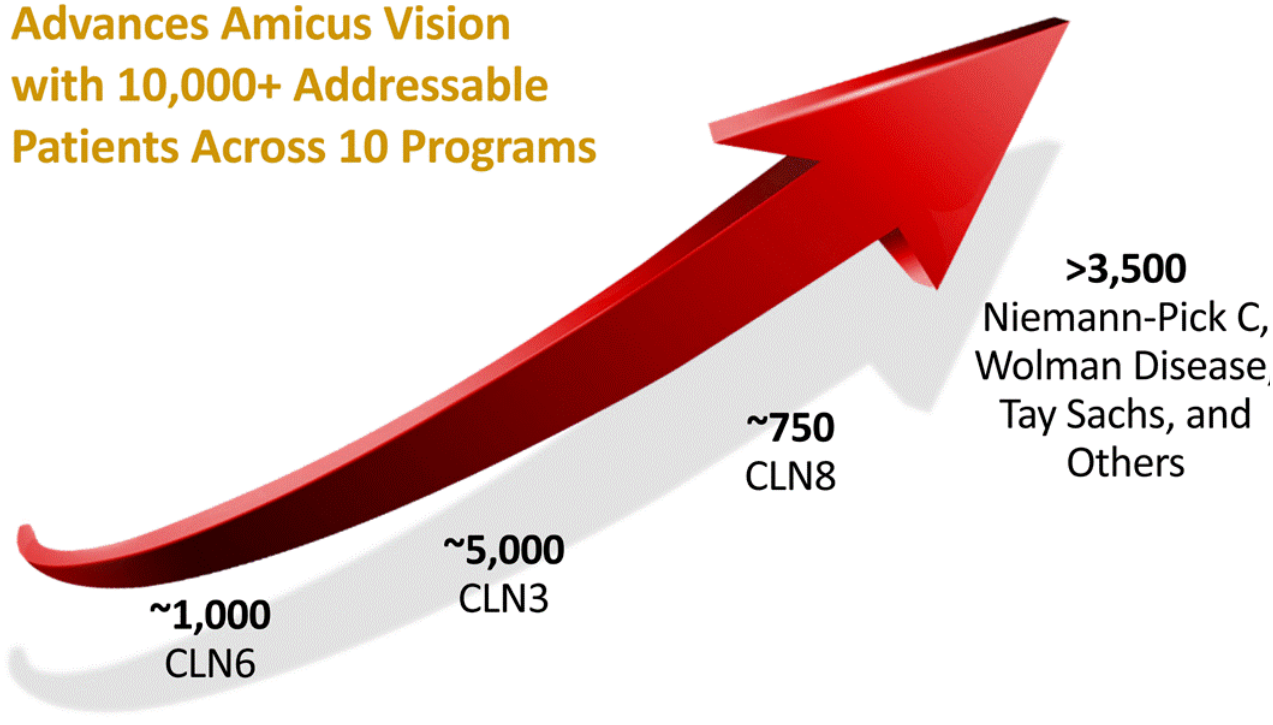
**Anticipating Multiple Program Milestones throughout 2018 & 2019**

- **First Patient in CLN3 Phase 1/2 Study**
- **Complete Enrollment in CLN6 Phase 1/2 Study**
- **Preliminary Phase 1/2 Data in CLN6**
- **Complete Enrollment in Initial Cohort in CLN3 Phase 1/2 Study**

Amicus AAV9 Gene Therapy Programs

# Addressable Patient Populations*

**Advances Amicus Vision with 10,000+ Addressable Patients Across 10 Programs**




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

# Q&A Session

John F. Crowley
Kathryn Meyer, Ph.D.
Jay Barth, M.D.
Jeff Castelli , Ph.D.



# Break

# Next Generation Gene Therapy Programs

Jeff Castelli, Ph.D.
Jim Wilson, M.D., Ph.D.
Hung Do, Ph.D.

*2018 Analyst Day | October 11, 2018 | Ne*

Amicus-Penn Collaboration

## Collaboration Overview

**Combines Amicus Expertise in Protein Engineering with Penn's AAV Vector Technology, Manuf Immunology Capabilities to Improve Safety and Efficacy and Speed Development**

- Dr. James Wilson and Gene Therapy Program (GTP) at UPenn: Renowned center of
  - >20 years of gene therapy experience
  - Proven platform with numerous clinical programs across multiple disease indications
  - Leader in next generation AAV technologies
- Strong synergy with Amicus' protein engineering capabilities
  - Leverages Amicus expertise in optimizing protein expression, secretion, stabilization and tar
- Strategic fit with Amicus R&D, Commercial and Manufacturing capabilities
- WW rights to 4 LSD programs

# The Gene Therapy Program at University of Pennsylvania

Jim Wilson, M.D., Ph.D

*2018 Analyst Day | October 11, 2018 | Ne*

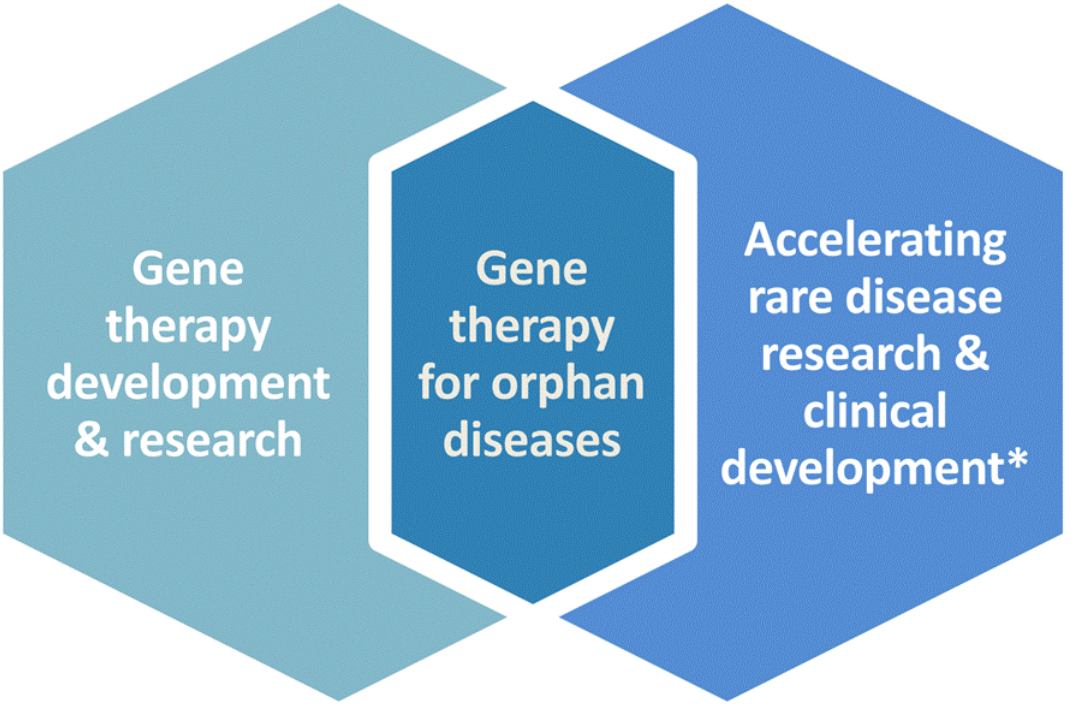
The **Orphan Disease Center** will develop **transformative** therapies using **platform** technologies that can be deployed across multiple rare diseases. We will emphasize disorders with substantial **unmet need** independent of their incidence and will strive to assure **access** to patients of all populations.

- Areas of emphasis for accelerating therapeutic development
- Establish and execute research agenda
- Partner with patient advocacy groups and create Alliances
- Engage in biopharmaceutical partnerships
- Early regulatory engagement
- Priority areas:
  - Lysosomal Storage Diseases
  - Infantile Epilepsies
  - Liver Metabolic Diseases
  - Neurodegenerative Diseases

the orpha diseas

# Symbiotic Relationship of Gene Therapy Program and Orphan Dise

GENE THERAPY PROGRAM




* thera

Amicus-Penn Collaboration

# Overview of GTP Vector Operations at Penn

Penn

## Numerous Vector Operations Become Available to Amicus as the Relationship Continue

### Clinical Vector Services

- Vector Manufacturing in support of pharm/tox IND-enabling studies
- Development of scalable upstream & downstream manufacturing processes
- Transfer of process technologies to CMOs
- Establishment of GMP manufacturing capabilities at GTP

### Analytics

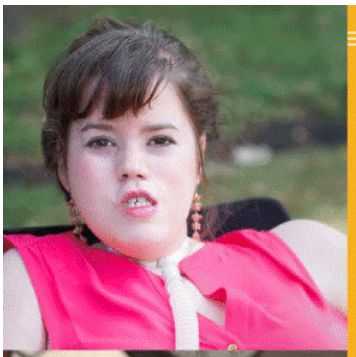
- GLP Quality Control of GMP and GMP process-comparable vectors
- Quality control of research vectors
- Development of assays for vector characterization and release
- Transfer of assay technologies to CMO/CROs

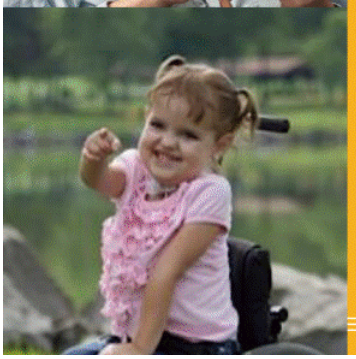
### Vector Design & Construction

- Design, construction & optimization of vector constructs
- Production & outsourcing of plasmid DNA source materials
- Structure & Sequence analysis of plasmid DNA
- Next generation sequencing (NGS) of plasmid source materials

### Precli S

- Producti vectors f preclinic
- Distribut 2.0 resea worldwi
- Manage transfer for outg materials
- IBC regis recombi





# Next Generation Gene Therapy Programs

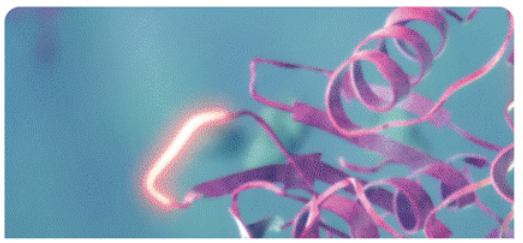

Jeff Castelli, Ph.D.
Jim Wilson, M.D., Ph.D.
Hung Do, Ph.D.


*2018 Analyst Day | October 11, 2018 | Ne*

Amicus-Penn Collaboration

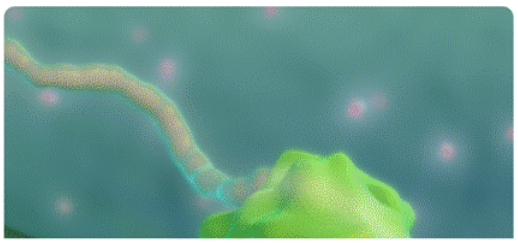
## Applying Amicus Protein Engineering Expertise and Technologies to Gene Therapy

**Enabling Greater Protein Expression and Delivery at Lower Gene Therapy D**



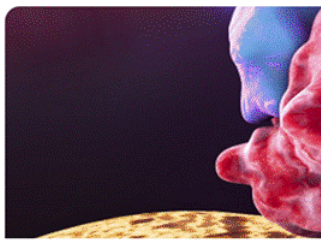
### Increased Protein Expression

Novel untranslated sequences to avoid inhibition of initiation and drive efficient protein synthesis



### Increased Protein Secretion

Effective signal sequences to increase protein expression & secretion



### Improved F Targeting and S

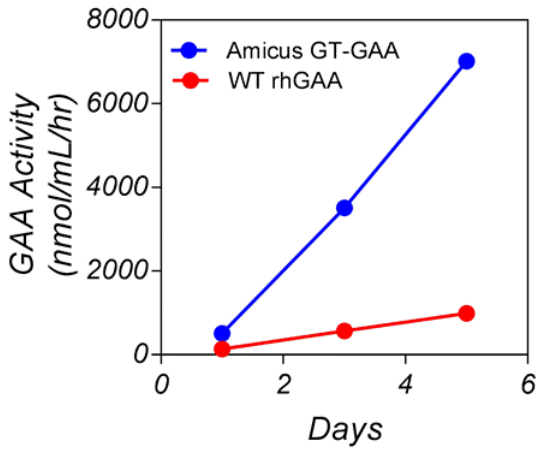
Targeting m

Protein de

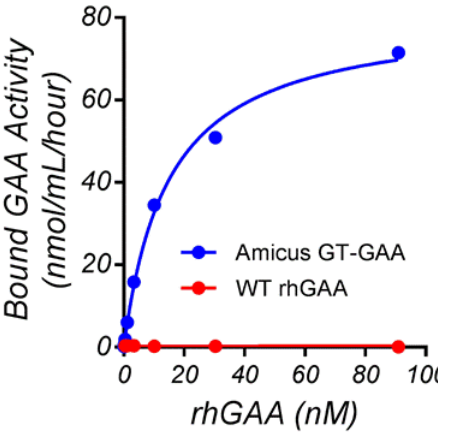
# Early Proof of Principle for Optimized Pompe Gene Therapy

## Amicus DNA Constructs Enable Highly Expressed GAA and Vastly Improved Cellular

### Secreted GAA in Media




### GAA Binding to Intended Re



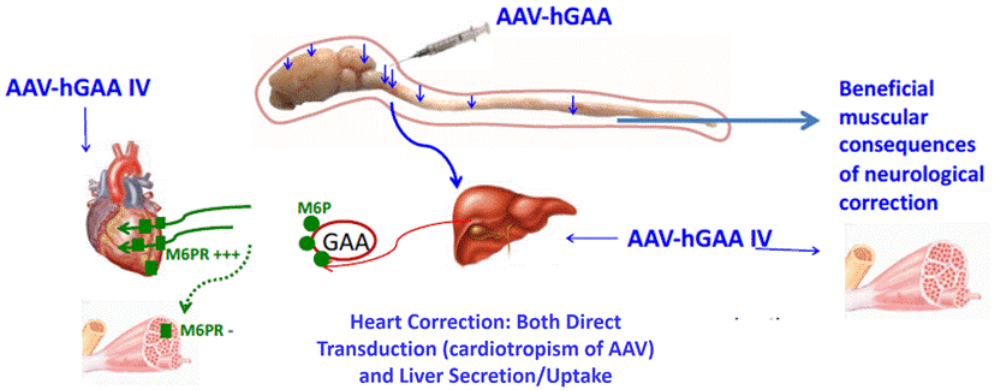



# Pompe Disease: AAV Gene Therapy Approach

## An Optimized Enzyme Delivered to Key Tissues May Correct both Central Nervous Musculoskeletal Aspects of Pompe to Address All Aspects of Disease

Aim : **Globally** Target and Correct the CNS, Heart, Muscles by AAV-hGAA Gene Therap

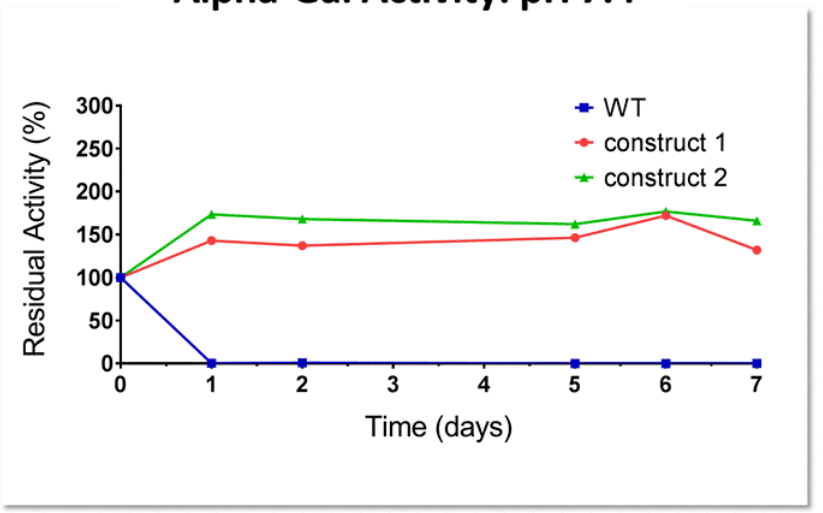
- Intravenous and/or intrathecal injection
- AAV : Neuronal + glial tropism, cardiac tropism, liver tropism



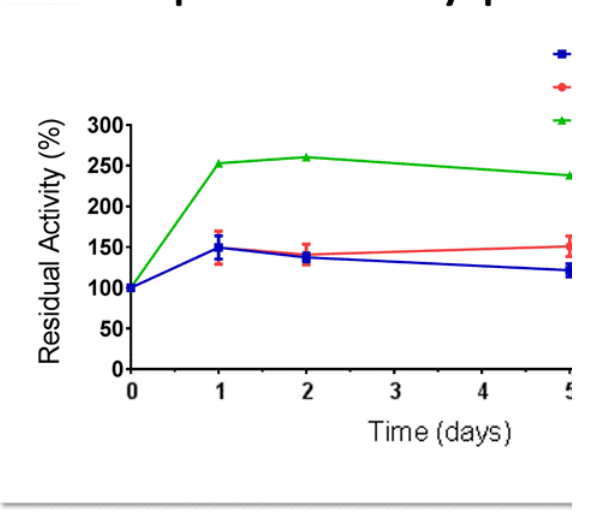
# Early Proof of Principle for Optimized Fabry Gene Therapy

## Amicus DNA Constructs Enable Highly Stable and Active α-Gal A Enzym

### Alpha-Gal Activity: pH 7.4




### Alpha-Gal Activity: pH 4.



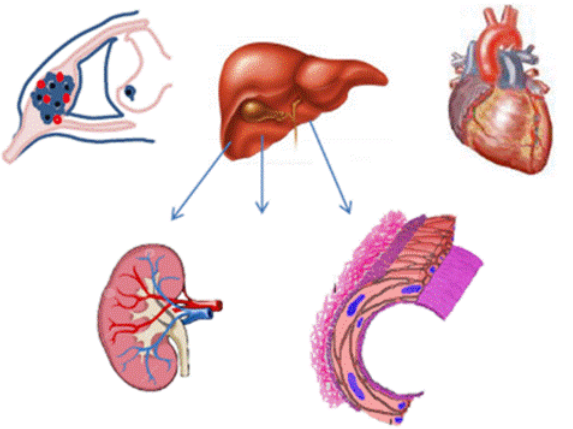

Amicus-Penn Collaboration

# Fabry Disease: AAV Gene Therapy Approach

## Goal is to Develop AAV Gene Therapies with Higher Transduction in Heart, Periph System and Liver with More Stable Enzyme and Better Uptake to Target Ti

Direct AAV robust transduction: in situ correction

Cross-correction from liver secretion

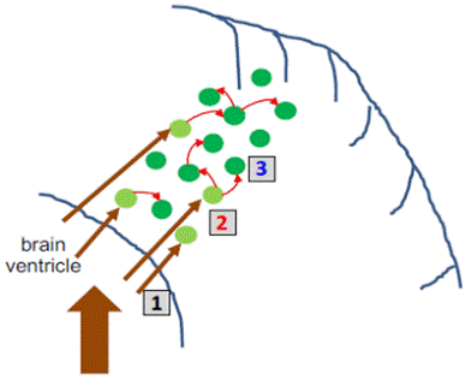


Liver targeted cross-correction: constant, high, steady enzyme levels
Heart and DRG tropism: direct in situ correction

# CDKL5 Deficiency Disorder (CDD) AAV Gene Therapy

## Utilizing an Amicus Cell Penetrating Peptide for Delivery of CDKL5 in Target Neu

**Goal:** ***Develop a clinical candidate for CDKL5 gene therapy with enhanced efficacy through CDKL5 secretion and uptake by neighboring neurons.***




Therapeutic Benefit
Increased expression of CDKL5 in the brain

# Q&A Session

**John F. Crowley**
**Hung Do, Ph.D.**
**Jeff Castelli, Ph.D.**
**Jim Wilson, M.D., Ph.D**

# First-in-human Study of ATB200/AT2221 in Patients With Pompe Disease: 18 Month Safety and Efficacy Dat From the ATB200-02 Trial


**Mark Roberts, M.D.**

Benedikt Schoser,[1] Drago Bratkovic,[2] Barry J. Byrne,[3] Paula Clemens,[4] Tarekegn Geberhiwot,[5] Ozlem Goker-Alpan,[6] Priya Kishnani,[7] Xue Ming,[8] Tahseen Mozaffar,[9] Pe Schwenkreis,[10] Kumaraswamy Sivakumar,[11] Ans T. van der Ploeg,[12] Jacquelyn Wright Swati Sathe,[13] Sheela Sitaraman,[13] Hjalmar Lagast,[13] Jay A. Barth,[13] Mark Roberts[14]

[1]Klinikum der Universität München-Neurologische Klinik, Friedrich-Baur-Institut, Munich, Germany; [2]PARC Research Clinic, Royal A Adelaide, SA, Australia; [3]University of Florida, Gainesville, FL, USA; [4]University of Pittsburgh and Department of Veterans Affairs Me PA, USA; [5]University Hospital Birmingham NHS Foundation Trust, Queen Elizabeth Medical Center, Birmingham, UK; [6]O&O Alpan L [7]Duke University Medical Center, Durham, NC, USA; [8]Rutgers New Jersey Medical School, Newark, NJ, USA; [9]University of Californ USA; [10]Neurologische Klinik und Poliklinik des Berufsgenossenschaftlichen, Universitätklinikum Bergmannsheil, Bochum, Germany; Research Center, Phoenix, AZ, USA; [12]Erasmus MC University Medical Center, Rotterdam, The Netherlands; [13]Amicus Therapeutic ; [14]Salford Royal NHS Foundation Trust, Salford, UK.



*2018 Analyst Day | October 11, 2018 | Ne*




## Disclosure Information

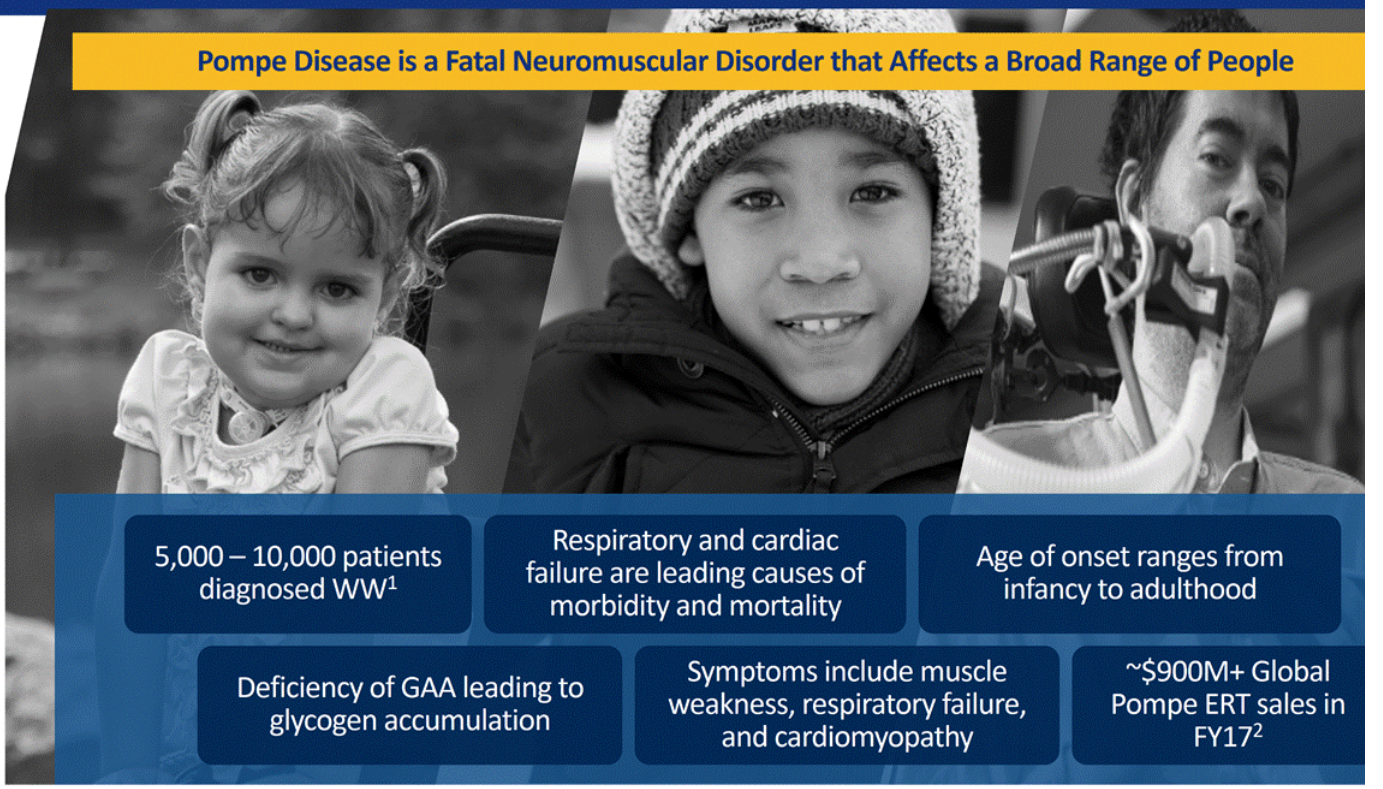
**I have the following financial relationships to disclose:**

- Consultant for Amicus Therapeutics, Inc.
- Consultant and member of speaker bureau for Audentes, Biomarin, and Sanofi

**I will discuss the following off-label use and/or investigational use in my presenta**

- Data from a phase 1/2 trial of ATB200/AT2221 for the treatment of patients with Po
- ATB200/AT2221 is an investigational therapy that has not been approved for comme

# Pompe Disease Overview

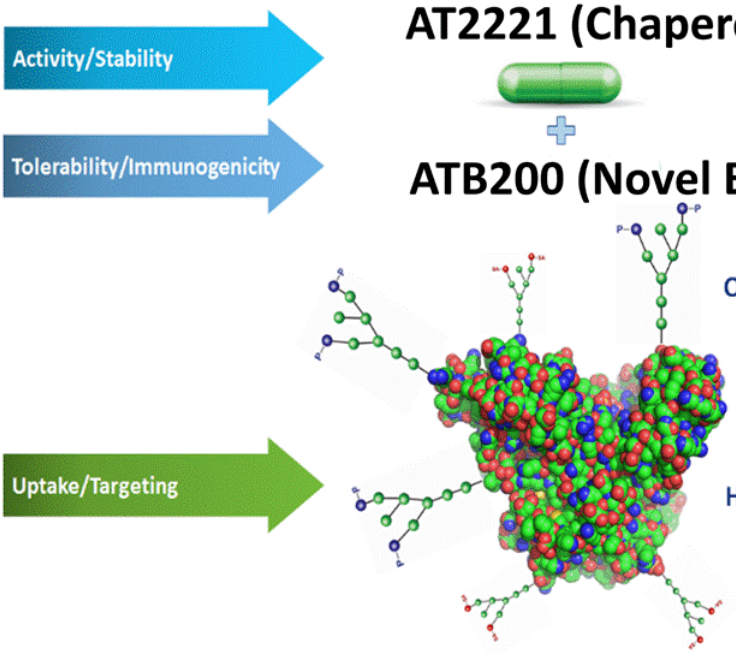



1. National Institute of Neurological Disorders and Stroke (NIH). 2. Sanofi Press Release & 10-K

Pompe 18 Month Data Highlights

# ATB200 Co-administration With AT2221

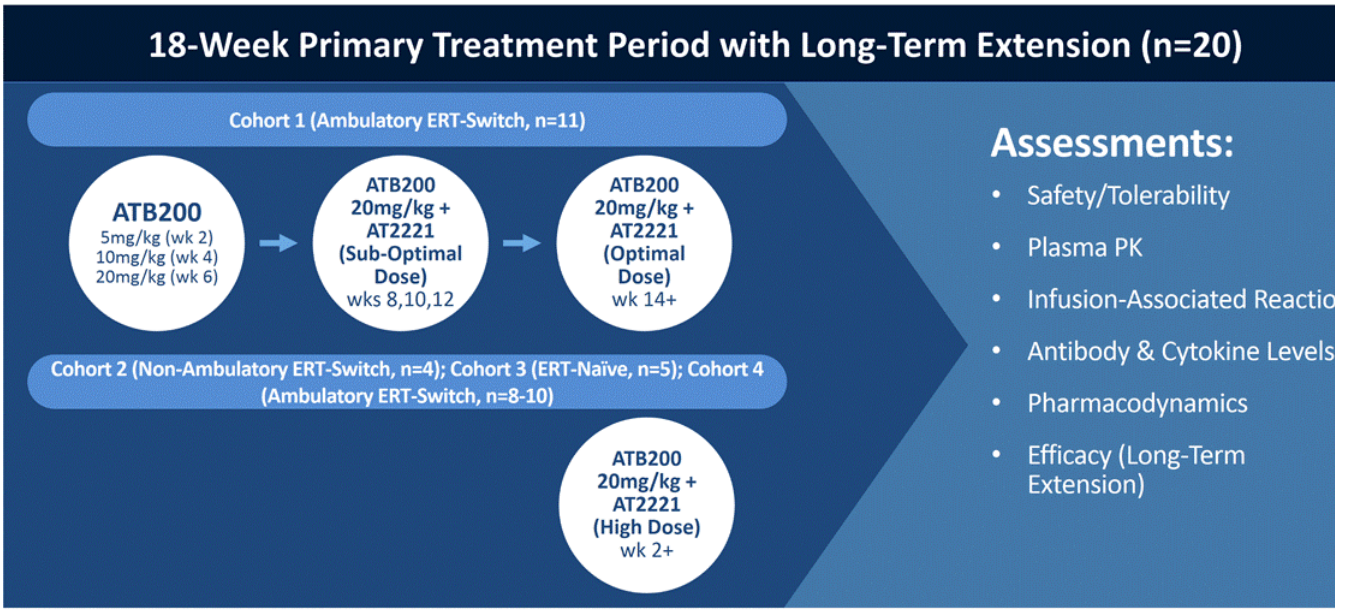
- AT2221: orally administered investigational PC prior to infusion of ATB200
  - Shown to stabilize ERT in blood and maintain catalytic activity to enhance delivery of active enzyme to lysosomes[1,2]
- ATB200: investigational next-generation ERT
  - Designed with optimized glycosylation and high levels of mannose 6-phosphate residues for better uptake to target tissues




M6P=mannose-6-phosphate; PC=pharmacologic chaperone.
1. Gotschall R et al. *Mol Genet Metab*. 2015;114(2):S49. Abstract 94. 2. Khanna R et al. Presented at: the 12th Annual WORLD*Symposium*™; February 29-March 4, 2016; San Di

# ATB200-02 Study Design (NCT02675465)

**Phase 1/2 Clinical Study to Evaluate Safety, Tolerability, Pharmacokinetics (PK), and Pharmacody**
**ATB200 + Chaperone (AT-GAA) at 16 Sites in 5 Countries**




*Cohort 1: Ambulatory ERT-Switch 2-6 yrs. on SOC, n=11; Cohort 4: Ambulatory ERT-Switch >7 yrs. On SOC , Planned n=8-10*

Pompe 18 Month Data Highlights

# Baseline Characteristics (N=20)

**Patients Enrolled Across Three Cohorts are Representative of the Overall Late-Onset Population, with Significant Impairment at Baseline**

| | Cohort 1 ERT-Switch (N=11[#]) | Cohort 2 ERT-Switch Non-ambulatory (N=4) | C E |
|---|---|---|---|
| Age, years, mean (min, max) | 49.4 (28, 66) | 36.0 (18, 56) | 49 |
| Sex, M:F | 9:2 | 3:1 | |
| Time on alglucosidase alfa, years, mean (SD) | 4.8 (1.42)[a] | 8.9 (3.8) | |
| 6MWT, meters, mean (SD) | 392.0 (93.4) | NA | 39 |
| FVC Upright, % predicted, mean (SD) | 52.3 (13.2) | NA | 53 |

6MWT=6-Minute Walk Test; FVC=forced vital capacity; LOPD=late-onset Pompe disease; NA=not applicable; SD=standard deviation.
[a]Cohort 1 patients were required to have been on alglucosidase alfa for 2-6 years at baseline. # One Cohort 1 patient discontinued after 18 weeks due to burden of travel

# 6-Minute Walk Test

## 6MWT Improved for Both ERT-switch Ambulatory and ERT-naive Patients at Month 6 with Continued Benefit Observed out to Month 18

| All results are mean (SD), meter | Baseline | Change From Baseline | | |
|---|---|---|---|---|
| | | Month 6 | Month 12 | |
| Cohort 1 ERT-Switch Ambulatory | n=10 | n=10 | n=10 | |
| | **397.2** (96.8) | **+23.9** (52.2) | **+42.2** (46.5) | |
| Cohort 3 ERT-Naive | n=5 | n=5 | n=5 | |
| | **399.5** (83.5) | **+41.8** (29.4) | **+63.1** (29.1) | |

- 6MWT increased in 7/10, 9/10, and 9/9 ERT-switch patients at Months 6, 12, and 18, respectively
- 6MWT increased in 5/5, 5/5, and 5/5 ERT-naive patients at Months 6, 12, and 18, respectively
- Timed motor function tests were consistent with 6MWT

6MWT=6-minute walk test; ERT=enzyme replacement therapy; SD=standard deviation. [a]Data for one patient is pending (visit had not occurred at ti

Pompe 18 Month Data Highlights

# 6-Minute Walk Test Patient-Level Data – Cohort 1 ERT-Switc

## 6MWT Improved for ERT-Switch Patients at Months 6, 9 and 12 With Continued Benefit Observed

### 6-Minute Walk Test (m)

| ID | Baseline | Change From Baseline | | |
|---|---|---|---|---|
| | | Month 6 | Month 12 | Month 1 |
| 1052 | 544 | +51 | +112 | +76 |
| 1252 | 379 | +125 | +103 | +147 |
| 1251 | 339 | +21 | +73 | +92 |
| 1751 | 332 | +8 | +45 | +29 |
| 1201 | 456 | -5 | +41 | +29 |
| 1451 | 500 | +55 | +33 | +24 |
| 1051 | 220 | +29 | +30 | +15 |
| 1053 | 410 | +38 | +22 | +50 |
| 1701 | 464 | -4 | +13 | +3 |
| 1601 | 328 | -78 | -50 | N/A |
| **Mean (SD)** | **397.2** (96.8) | **+23.9** (52.2) | **+42.2** (46.5) | **+51.7** (45.9) |

➢ 6MWT increased in 7/10, 9/10, and 9/9 ERT-switch patients at Months 6, 12, and 18, respecti

N/A = data not available (patient has not reached 18 month time point)

# 6-Minute Walk Test Patient Level Data – Cohort 3 ERT-Naïve

## All Five ERT-Naive Patients Showed Increases in 6MWT Distance Out to Month 18

### 6-Minute Walk Test (m)

| ID | Baseline | Change From Baseline | | |
|---|---|---|---|---|
| | | Month 6 | Month 12 | Month 18 |
| 3551 | 480 | +41 | +95 | +82 |
| 3552 | 384 | +62 | +79 | +74 |
| 3051 | 460 | +79 | +78 | +43 |
| 3554 | 406 | +14 | +33 | +33 |
| 3553 | 267 | +13 | +31 | +14 |
| **Mean (SD)** | **399.5** (83.5) | **+41.8** (29.4) | **+63.1** (29.1) | **+49.0** (28.3) |

6MWT increased in 5/5, 5/5, and 5/5 ERT-naive patients at Months 6, 12, and 18, respectively

N/A = data not available (patients have not reached 18 month time point)

Pompe 18 Month Data Highlights

# Timed Motor Function Tests

## Improvement in Other Motor Function Tests was Generally Consistent for Both ERT-switch and ER over 18 months

| | Test | Baseline, mean (SD) | Change From Baseline, m | |
|---|---|---|---|---|
| | | | Month 6 | Month 12 |
| Cohort 1 ERT-Switch Ambulatory | | n=10 | n=10 | n=10 |
| | Timed Up and Go, sec | **10.5** (6.6) | **−1.8** (3.5) | **-1.5** (2.8) |
| | GSGC Score | **12.6** (4.8) | **+0.1** (3.9) | **-0.3** (4.1) |
| Cohort 3 ERT-Naive | | n=5 | n=5 | n=5 |
| | Timed Up and Go, sec | **9.4** (2.3) | **−1.0** (1.1) | **-0.8** (2.5) |
| | GSGC Score | **12.2** (3.6) | **−1.8** (3.8) | **-0.3** (1.9) |

**one subject had difficulty with this assessment at month 18 (fall/hernia week prior to assessment) and the median CFBL was -1.5 seconds*

GSGC=Gait, Stairs, Gowers, Chair. GSGC is an observer-rated combined score of 4 motor function assessments: Gait (10-meter walk), 4-Stair Climb, Gowers (Stand From Floor), and Rising Fro a scale of 1 (normal) to 7 (cannot perform, max score 6 for rising from chair). Total scores range from 4 to 27.

# Manual Muscle Strength Testing: Cohorts 1, 2 and 3

## Increases Were Observed in Manual Muscle Strengths in All Patients Out to Month 1

| | Body Area | Baseline | | Change From Baseline | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Month 6 | | Month 12 | | |
| | | mean (SD) | n | mean (SD) | n | mean (SD) | n | m |
| ERT-switch Ambulatory | Total Body Max score 80 | 66.4 (8.1) | 10 | +2.5 (3.2) | 9 | +3.3 (3.4) | 9 | + |
| ERT-switch Non-Ambulatory | Upper Body Max score 40 | 13.3 (12.2) | 3[b] | +4.5 (0.7) | 2[bc] | +2.7 (2.3) | 3[b] | + |
| ERT-Naive | Total Body Max score 80 | 66.9 (3.7) | 5 | +0.3 (2.8) | 5 | +1.1 (3.1) | 5 | + |

ERT=enzyme replacement therapy; SD=standard deviation. [a]Measured via the Medical Research Criteria (MRC) scale; [b]Baseline data missing for complete Month 6 assessment; [d]Manual muscle testing not completed for one patient; [e]Measured via hand-held dynamometer.

Pompe 18 Month Data Highlights

# Quantitative Muscle Strength Testing: Cohorts 1, 2 and

## Increases were Observed in Quantitative Muscle Strength (Dynamomet in All Cohorts Out to Month 18

| *All results are mean (SD), lbs* | Baseline | | Change From Baseline | | | | |
|---|---|---|---|---|---|---|---|
| | | | Month 6 | | Month 12 | | Mo |
| | mean (SD) | n | mean (SD) | n | mean (SD) | n | mean |
| Cohort 1 ERT-Switch Ambulatory | 33.0 (11.5) | 10 | **-0.7** (7.0) | 10 | + 0.7 (7.0) | 10 | +1.3 ( |
| Cohort 2 ERT-Switch Nonambulatory | 6.5(7.0) | 4 | +1.6 (4.9) | 4 | +3.3 (4.0) | 4 | +3.6 ( |
| Cohort 3 ERT-Naive | 21.5(6.5) | 5 | +0.9 (2.5) | 5 | **-0.1** (4.1) | 5 | +1.8 ( |

** QMT not performed for one patient at M18*

# Sitting Forced Vital Capacity (FVC, % Predicted)

**FVC Increased In ERT-Naïve Patients and was Generally Stable in ERT-Switch Patien**

| | Baseline, mean (SD) | Change From Baseline, mean (SD) | | |
|---|---|---|---|---|
| | | Month 6 | Month 12 | Month 18 |
| Cohort 1 ERT-Switch Ambulatory | n=9[a] | n=9[a] | n=9[a] | n=8[a,b] |
| | **52.6** (14.7) | **−1.3** (4.1) | **−3.3** (6.1) | **−3.7** (7.0) |
| Cohort 3 ERT-Naive | n=5 | n=5 | n=5 | n=5 |
| | **53.4** (20.3) | **+4.2** (5.6) | **+4.4** (8.6) | **+5.0** (2.9) |

ERT=enzyme replacement therapy; SD=standard deviation.
[a]Baseline FVC not available for 1 patient in Cohort 1; [b]FVC for one patient in Cohort 1 pending (visit had not occurred at time of interim data cut). .

Pompe 18 Month Data Highlights

# Other Pulmonary Function Tests: MIP and MEP

**MIP was stable and MEP increased in ERT-switch patients;**
**MIP and MEP increased in ERT-naive patients**

| | Assessment | Baseline, mean (SD) | Change From Baseline, m | |
|---|---|---|---|---|
| | | | Month 6 | Month 12 |
| Cohort 1 ERT-Switch Ambulatory | | n=10 | n=10 | n=10 |
| | MIP | **35.7** (11.0) | **+0.3** (4.6) | **0.0** (3.2) |
| | MEP | **72.6** (32.6) | **+16.1** (42.1) | **+28.6** (44.0) |
| Cohort 3 ERT-Naive | | n=5 | n=5 | n=5 |
| | MIP | **32.6** (18.5) | **+11.0** (5.0) | **+5.2** (12.2) |
| | MEP | **60.6** (8.3) | **−0.4** (12.4) | **+8.6** (16.3) |

ERT=enzyme replacement therapy; MEP=maximal expiratory pressure; MIP=maximal inspiratory pressure; SD=standard deviation.
MIP and MEP measured in centimeters of water.
[a]Data for one patient in Cohort 1 pending (visit had not occurred at time of interim data cut).

# Fatigue Severity Scale (FSS)

## All Cohorts were Significantly Impacted by Fatigue at Baseline and Demonstrated a Mean Improve

| | Baseline, mean (SD) | Change From Baseline, mean ( | |
|---|---|---|---|
| | | Month 6 | Month 12 |
| Cohort 1 ERT-Switch Ambulatory | n=10 | n=10 | n=10 |
| | **53.5** (7.7) | **−8.0** (10.7) | **−8.0** (6.5) |
| Cohort 2 ERT-Switch Nonambulatory | n=4 | n=4 | n=4 |
| | **42.3** (14.6) | **+2.3** (8.7) | **−12.5** (10.0) |
| Cohort 3 ERT Naive | n=5 | n=5 | n=5 |
| | **39.2** (12.7) | **−5.2** (11.7) | **−7.2** (7.5) |

ERT=enzyme replacement therapy; SD=standard deviation.

1. Grace J et al. *Parkinsonism Relat Disord*. 2007;13(7):442-445.

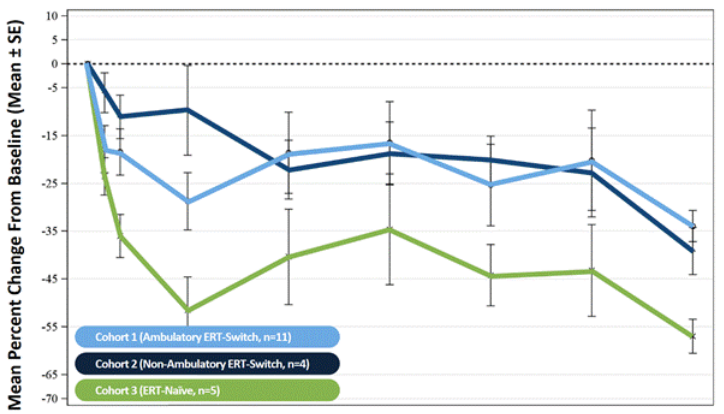
FSS consists of 9 questions, each scored on a scale from 1 to 7. Total scores range from 9 to 63, with higher values representing higher levels of fa condition. The normative value in the healthy population is ~21.[1]



# CK and Hex4 Biomarkers

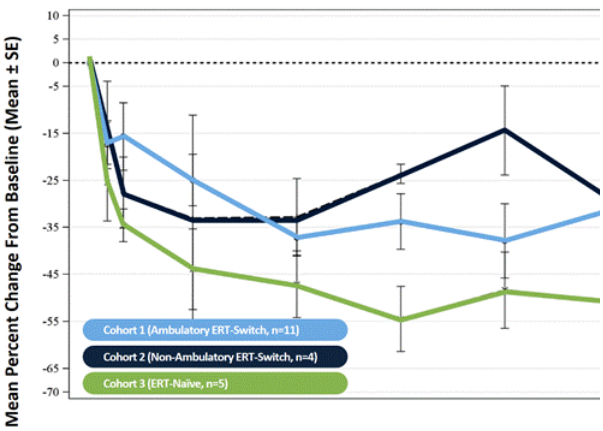
## All Cohorts Demonstrated Persistent Improvement in Biomarkers of Muscle Damage ( Disease Substrate (Hex4) For Up To 18 Months

### Percent Change from Baseline for CK




| Visit | BL | WK 2 | WK 4 | M3 | M6 | M9 | M12 | M15 | M18 |
|---|---|---|---|---|---|---|---|---|---|
| N | 11,4,5 | 11,4,5 | 10,4,4 | 8,3,5 | 10,4,5 | 10,4,5 | 8,1,2 | 9,4,3 | 8,3,3 |

### Percent Change from Baseline for Hex 4




| Visit | BL | WK 2 | WK 4 | M3 | M6 | M9 | M12 |
|---|---|---|---|---|---|---|---|
| N | 11,4,5 | 11,4,5 | 11,4,5 | 11,4,5 | 10,4,5 | 9,4,5 | 7,1,2 |

CK=creatine kinase; Hex4=urine hexose tetrasaccharide.

Missing values either unable to be analyzed or not yet analyzed.

# Safety Summary

**Safety data (N=20) for AT-GAA Show that AEs Have Been Generally Mild and Transient wi**
**Rates of IARs (<1%) after 890+ Total Infusions Across All Cohorts**

- AEs were generally mild and transient
  - The most common treatment-emergent AEs[a] by decreasing frequencies were nasopharyngitis (10/20); fall (9/20); abdomina (8/20); upper respiratory tract infection (7/20); arthralgia, nausea, fatigue, pain in extremities, and myalgia (6/20); and head oropharyngeal pain, and muscle spasms (5/20)
- For SAEs, 5 events occurred in 4 patients (severity: 3 moderate, 2 mild) and were unrelated to treatment. SAEs did nc interruption or study discontinuation.
- 7 incidents of IARs in 5 patients in 890+ infusions, which were controlled by standard medication or premedication
  - 1 IAR event each in 3 ambulatory ERT-switch patients
  - 1 IAR event in a non-ambulatory ERT-switch patient
  - 3 IAR events in a ERT-naive patient
- Longest duration of treatment is 28+ months

AE, adverse events; ERT=enzyme replacement therapy; IAR, infusion-associated reaction; SAE=serious adverse event.
[a]Number of patients experiencing the AE; [b]Includes upper and lower abdominal pain.

Pompe 18 Month Data Highlights

# Conclusions at 18 Months of Treatment

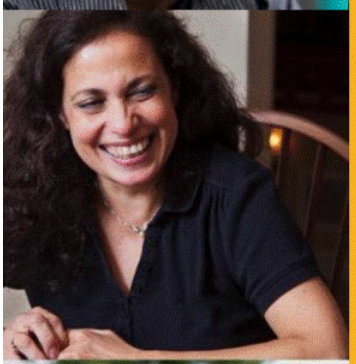
- 6MWT showed continued benefit in ERT-naïve and ERT-switch patients
- Timed motor function tests were generally consistent with 6MWT results in both a cohorts
- Muscle strength increased in all cohorts, including nonambulatory ERT-switch pati
- Pulmonary function
  - FVC, MIP, and MEP generally increased in ERT-naive patients
  - FVC, MIP, and MEP were generally stable in ERT-switch patients
- Fatigue Severity Scale
  - Improvement in fatigue score was observed in all cohorts
- Biomarkers and Safety
  - CK and Hex4 levels decreased in all cohorts
  - AT-GAA (ATB200/AT2221) was generally well tolerated

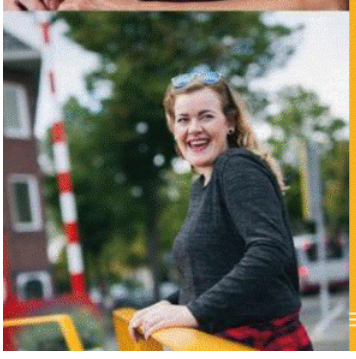
6MWT=6-minute walk test; CK=creatine kinase; ERT=enzyme replacement therapy; FVC=forced vital capacity; Hex4=urine hexose tetrasaccharide; MEP=maximal expiratory pressure; MIP=maximal inspiratory pressure.

# Amicus Patient Advocacy & Patient Perspectives


Jayne Gershkowitz, Chief Patient Advocate
George Fox, Pompe Caregiver to son Phoenix
Mike Stanzione, Living with Pompe


*2018 Analyst Day | October 11, 2018 | Ne*





**Amicus Therapeutics is committed to improving the lives of patients and familie affected by rare and orphan diseases.**

*- Belief Stateme*

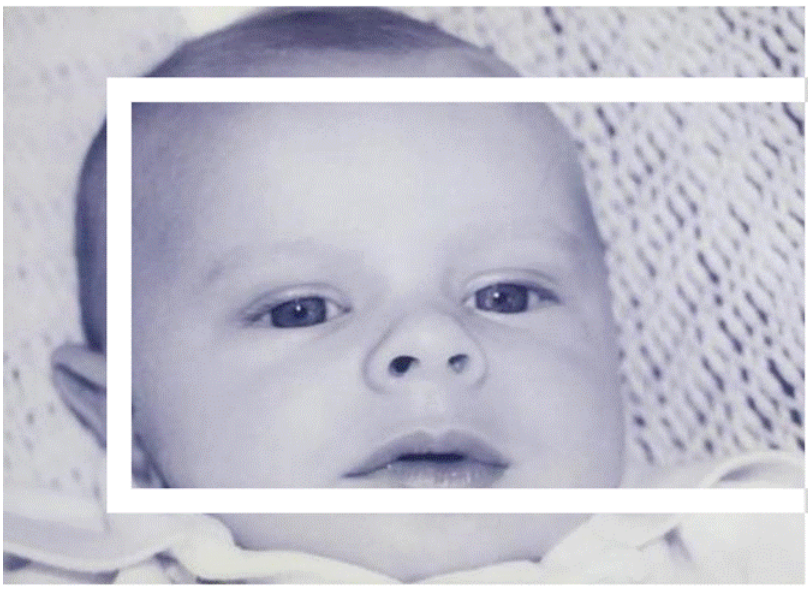
# What Drives Our Dedication

**We are driven by the journeys, experiences, involvement, relationships and outcomes of individuals and families living with rare disease.**

# Personal Perspectives on Pompe

**George Fox, Dad and Caregiver to son, Phoenix**

# A Pompe Caregiver's Perspective: George Fox



George Fox's son Phoenix

Pompe Patient Perspectives

# A Pompe Caregiver's Perspective: George Fox

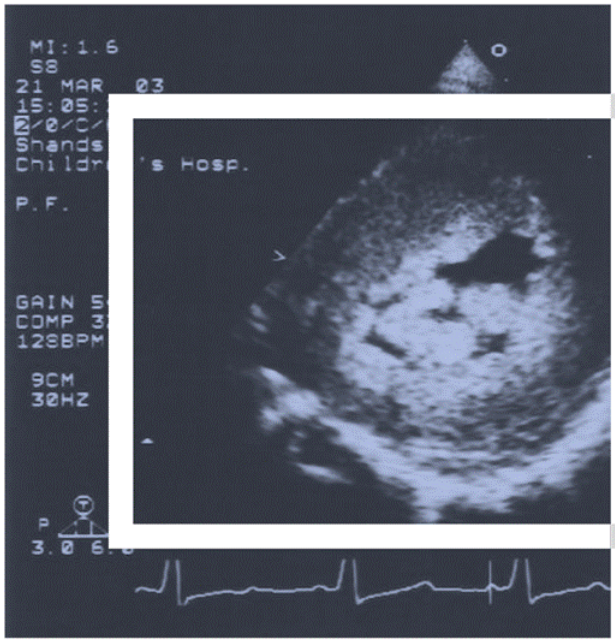
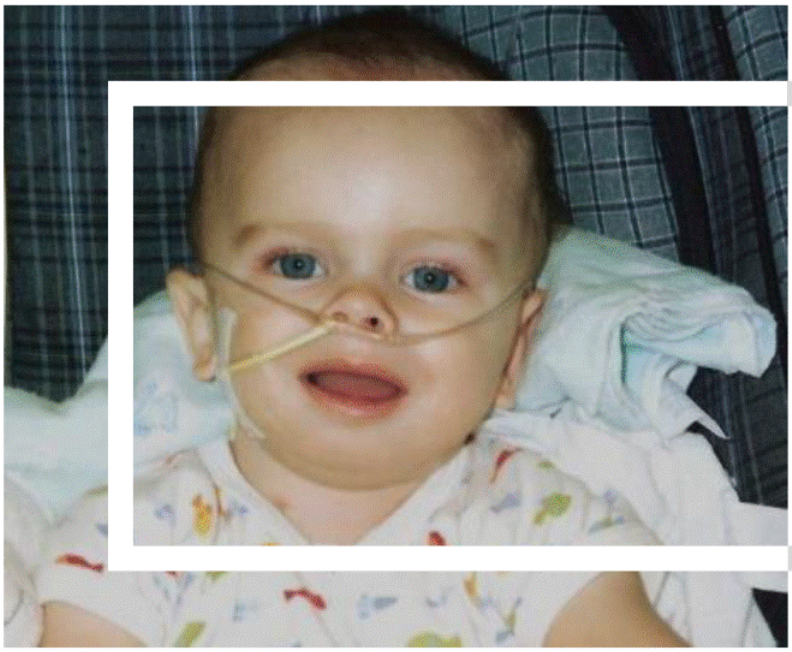



Image of Phoenix' enlarged heart in 2003 at 8 months old, a result of his Pompe disease.

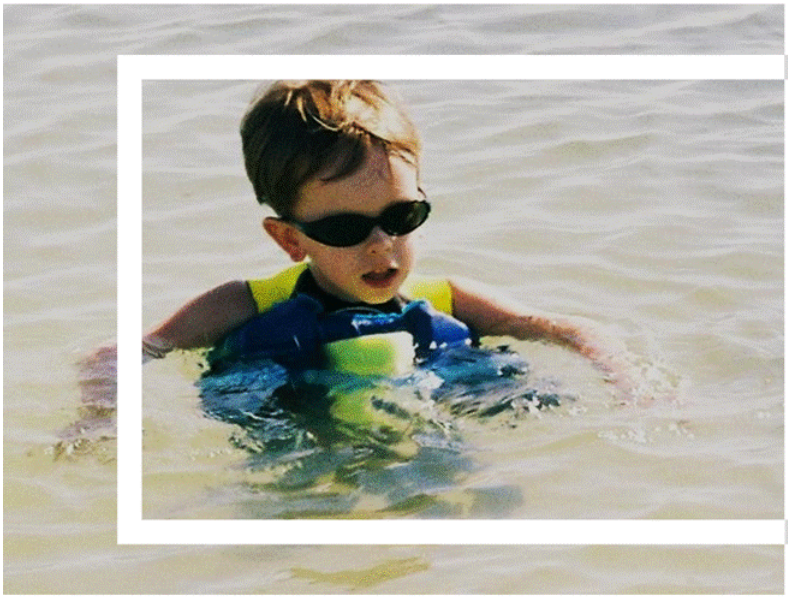
# A Pompe Caregiver's Perspective: George Fox



**Phoenix at diagnosis.**

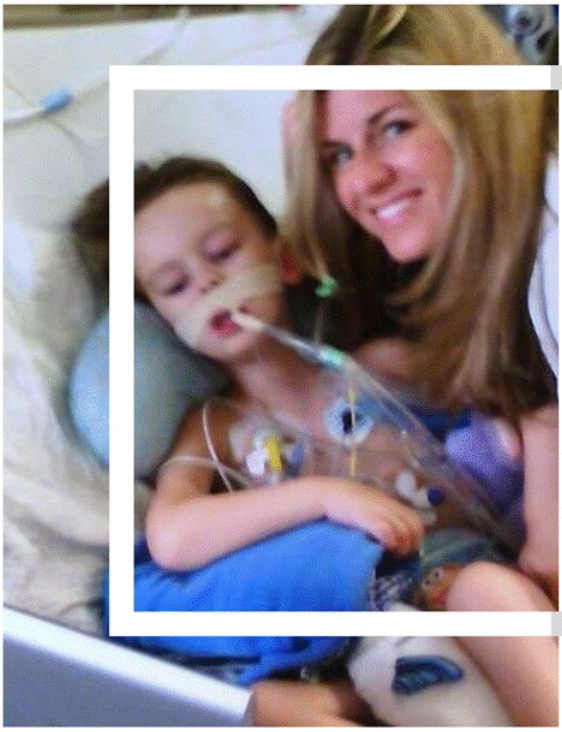
Pompe Patient Perspectives

A Pompe Caregiver's Perspective: George Fox



**Phoenix swimming; Standing in the water for the first time**

# A Pompe Caregiver's Perspective: George Fox



**Phoenix develops pneumonia and goes on ventilator at 3 years old**

Pompe Patient Perspectives

A Pompe Caregiver's Perspective: George Fox

**Phoenix enjoying the zoo with Dad.**

# A Pompe Caregiver's Perspective: George Fox

**Phoenix swimming at age 10 years old**

Pompe Patient Perspectives

A Pompe Caregiver's Perspective: George Fox

**Phoenix fishing.**

# A Pompe Caregiver's Perspective: George Fox

Phoenix greeting dolphins.

Pompe Patient Perspectives

A Pompe Caregiver's Perspective: George Fox


Fox Family at Jerry Lewis MDA Telethon. Phoenix Fox Foundation raises money for research or clinical care for folks with neuromuscular disease

# A Pompe Caregiver's Perspective: George Fox

Fox family out for a run;
Phoenix at 16 years old

# Personal Perspectives on Pompe

Mike Stanzione, Living with Pompe

*2018 Analyst Day | October 11, 2018 | Ne*

# Potential to Shift Treatment Paradigm for Pompe Disease

John F. Crowley

*2018 Analyst Day | October 11, 2018 | Ne*

AT-GAA Novel ERT + Chaperone for Pompe Disease

## Key Activities in 2018

### Significant Progress toward Clinical, Regulatory, and GMP Manufacturi Activities in 2018

**Year-to-Date Progress**

**CLINICAL**

- ☑ Addt'l. Phase 1/2 ATB200-02 extension data presented at WORLD*Symposium*
- ☑ Addt'l. patients in Phase 1/2 ATB200-02 clinical study
- ☑ Initiation of retrospective natural history of ERT-treated patients
- ☑ Prospective data collection on current ERT-treated patients
- ☑ 18-month data from ATB200-02 clinical study (4Q18)
- ☐ Initiation of larger registration-directed study
- ☐ Completion of a retrospective natural history study (2H18)

**REGULATORY**

- ☑ EMA: Received Scientific Advice Working Party Guidance
- ☑ U.S. FDA type C meeting and US update

**MANUFACTURING**

- ☑ Final FDA agreement on comparabi 1,000L and 250L GMP scale
- ☑ German regulatory authorities (BfA on strategy to demonstrate compa 1,000L and 250L GMP scale
- ☑ Release for clinic of 1,000L GMP co material
- ☐ Announce plan for long term comm manufacturing

# Q&A Session

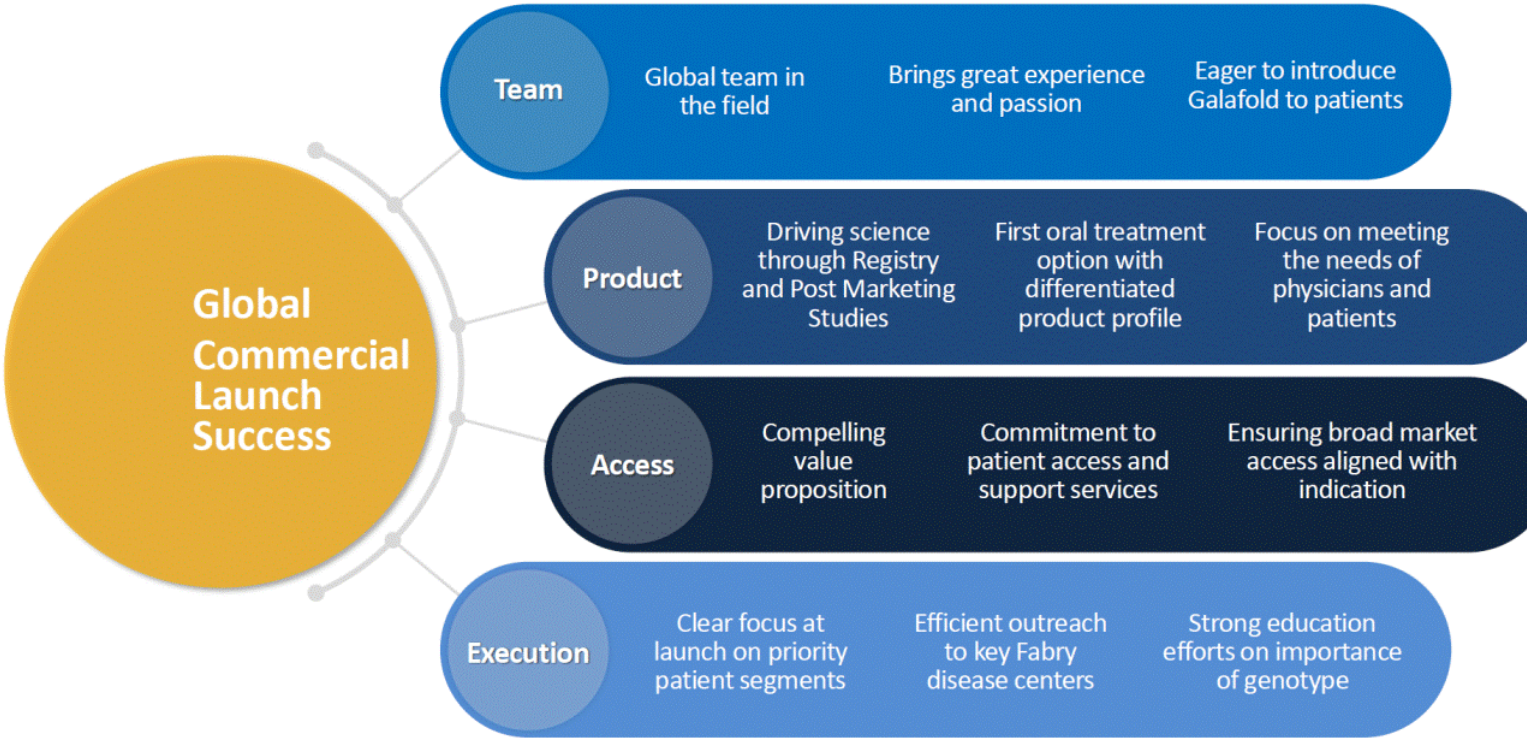
John F. Crowley
Jayne Gershkowitz
Mark Roberts, M.D.



# Galafold for Fabry Disease

Detlef Wolff
Bradley Campbell

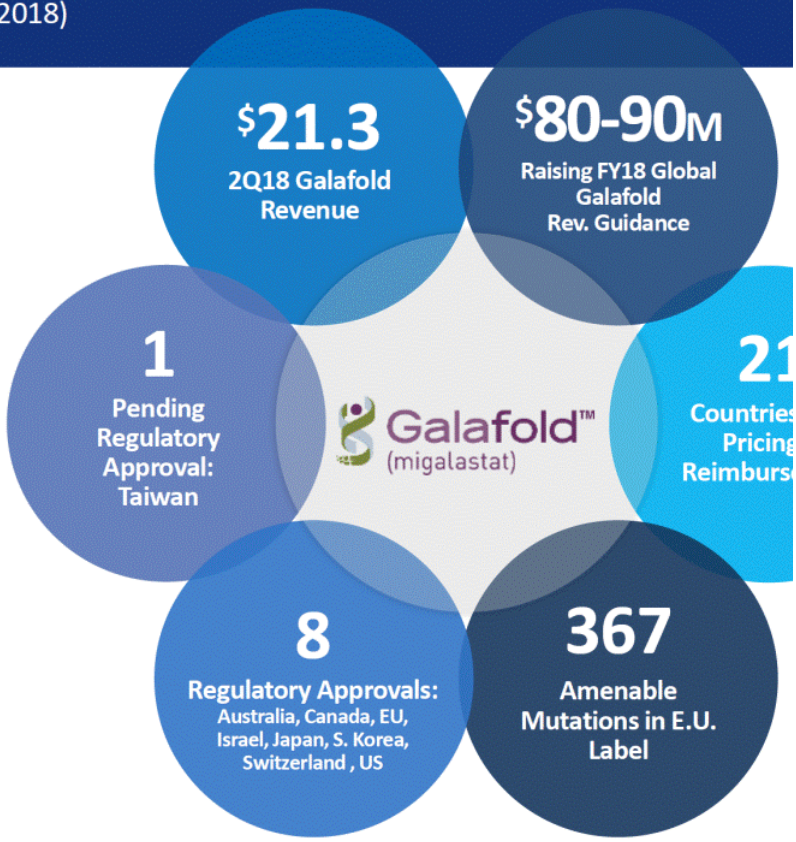
# Leveraging Our Operations Excellence




Galafold: Precision Medicine for Fabry Disease

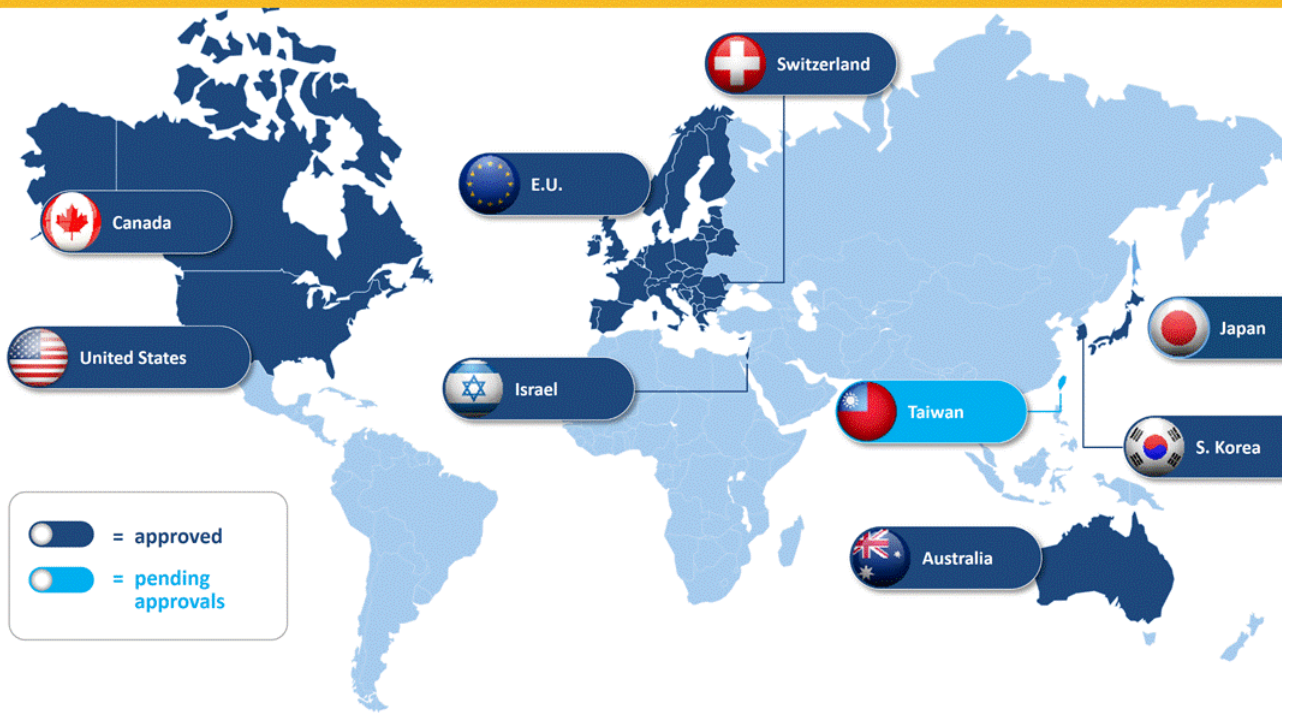
# Galafold Snapshot (as of October 11, 2018)

**FIRST Oral Precision Medicine for Fabry Disease Patients with Amenable Variants**



# Galafold Snapshot (as of October 11, 2018)

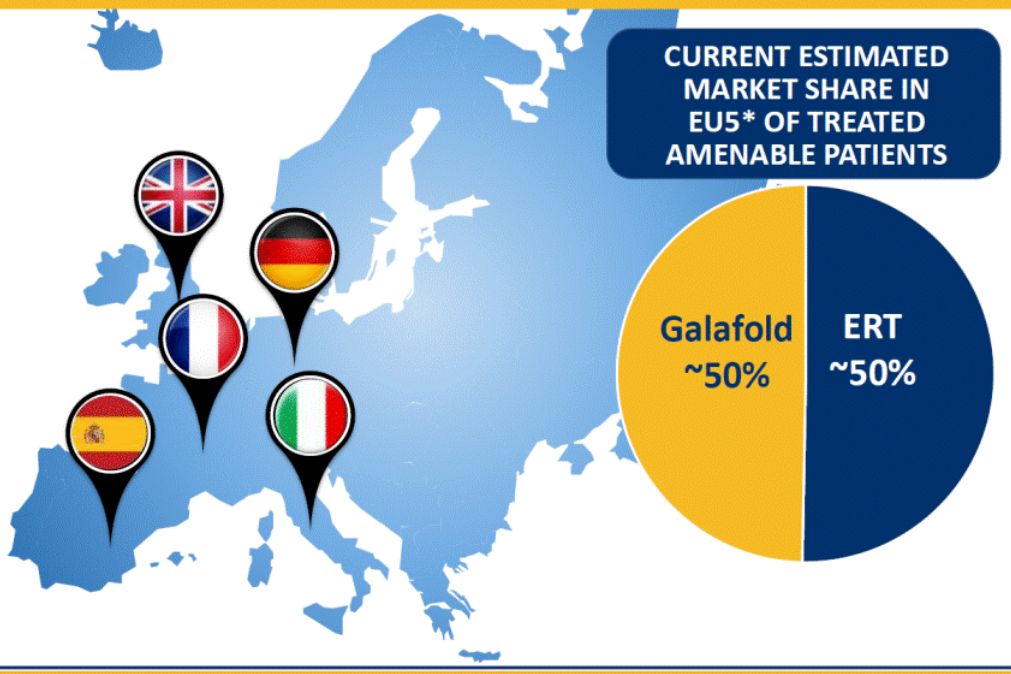
## Launched in Majority of Target Geographies with Continued Expansion into LatAm and S




Galafold: Precision Medicine for Fabry Disease

# International Update (as of October 11, 2018)

## Continuing to Execute on Our Strategy with High Compliance and Adhere
## Among 500+ patients on Galafold (Ex-U.S.)




**MARKET DYNA**

- Continued strong uptak patients
- Significant growth oppo diagnosed untreated pa
- Very high rates of adher compliance (>90%)
- Balanced mix of males a classic and late-onset pa
- Oral ROA allows for new patterns and seasonality
- Continued strong intere physician community
- ~150 HCPs attending up Fabry Meeting in Madri

*Market share assumptions based on estimated number of treated amenable patients in EU5 as of October 2018

# Japan Launch Update

## Japan Launch on Track and Setting Foundation for Significant Growth in 2019

- First commercial patients commenced treatment in late 2Q18
- Double digit number of patients now on Galafold
- ~900 patients diagnosed (>750 treated with an ERT)*
- No ERT home infusion currently available
- Broad interest from a wide set of KOLs / Treatment Centers

*Clinical & commercial, all figures approximate

Galafold: Precision Medicine for Fabry Disease

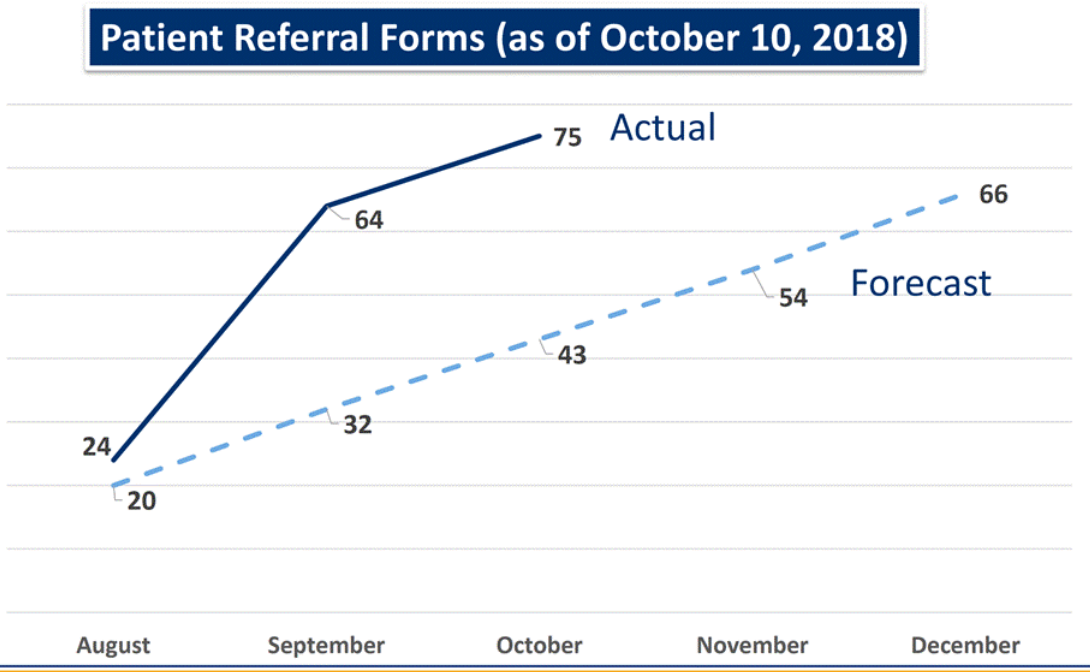
# U.S. Progress in First 8 Weeks of Launch

## Significant Demand for Galafold Seen in Early Days of U.S. Launch Sets a Strong Foundation for 2019

- Majority of clinical trial patients converting seamlessly to approved drug
- Majority of initial uptake in switch patients consistent with successful international strategy
- Longer term, market dynamics may enable faster uptake in naive patients
- Early approvals (Fairly Priced, Broadly Accessible) from both commercial and government payers
- Amicus assist™ running smoothly in support of reimbursement process
- Similar patient demographics and market dynamics as International

# Key U.S. Launch Metric

## Patient Referral Forms (PRFs) Significantly Exceed Initial Full-Year Forecast 8 Weeks




- PRF rate reflec demand
- Initial ~60 day to shipment t FY18 revenue
- Solid foundati

Galafold: Precision Medicine for Fabry Disease

# Galafold Success and FY18 Galafold Revenue Guidance

## International Launch Achieved Significant Growth in 2018 and Sets Foundation

# Total Amenable Patient Population ("TAPP")

Estimate based on 35% - 50% amenability

**Upside Po**

**WORLDW**

Diagnosis gr
to newborn s
in U.S. & J

**TAPP: 4,70**

$1B+ in 2019E-2023E in Cumulative Revenue Supporting R&D Investment

**Peak Potential**

**WORLDWIDE**

Diagnosis continues at current rate

**TAPP: 4,200-6,000**

**Today**

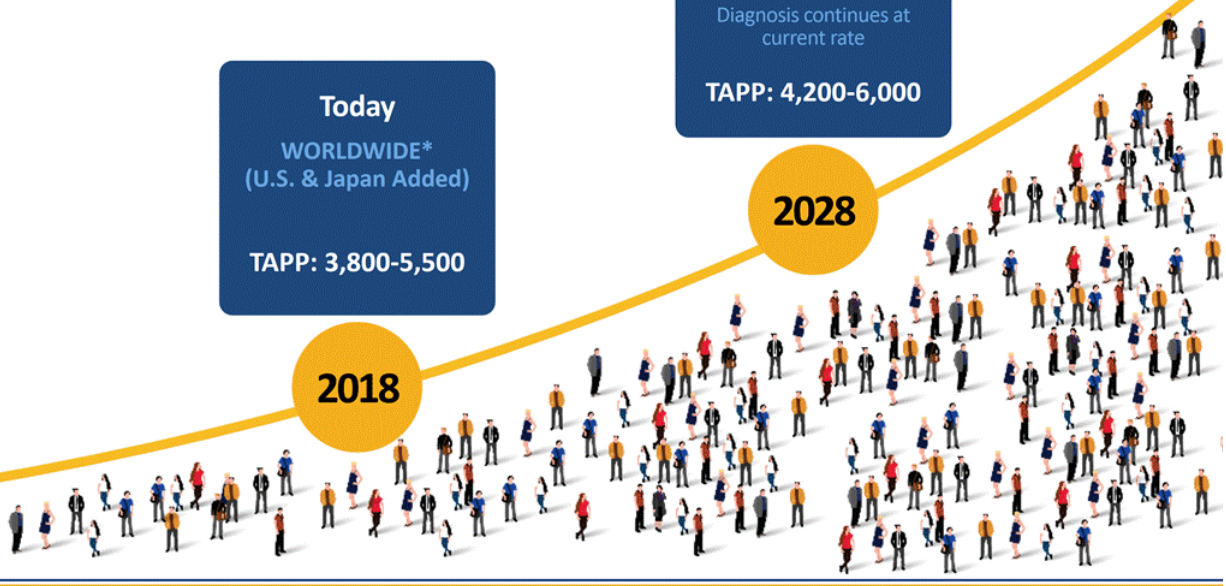
**WORLDWIDE***
**(U.S. & Japan Added)**

**TAPP: 3,800-5,500**

EU & ROW Only

**TAPP: 2,000-3,000**

**2017** **2018** **2028**



*WORLWIDE includes total amenable patient population in all Fabry ERT commercial markets today Estimated effect of newborn

# Closing Remarks

## John F. Crowley

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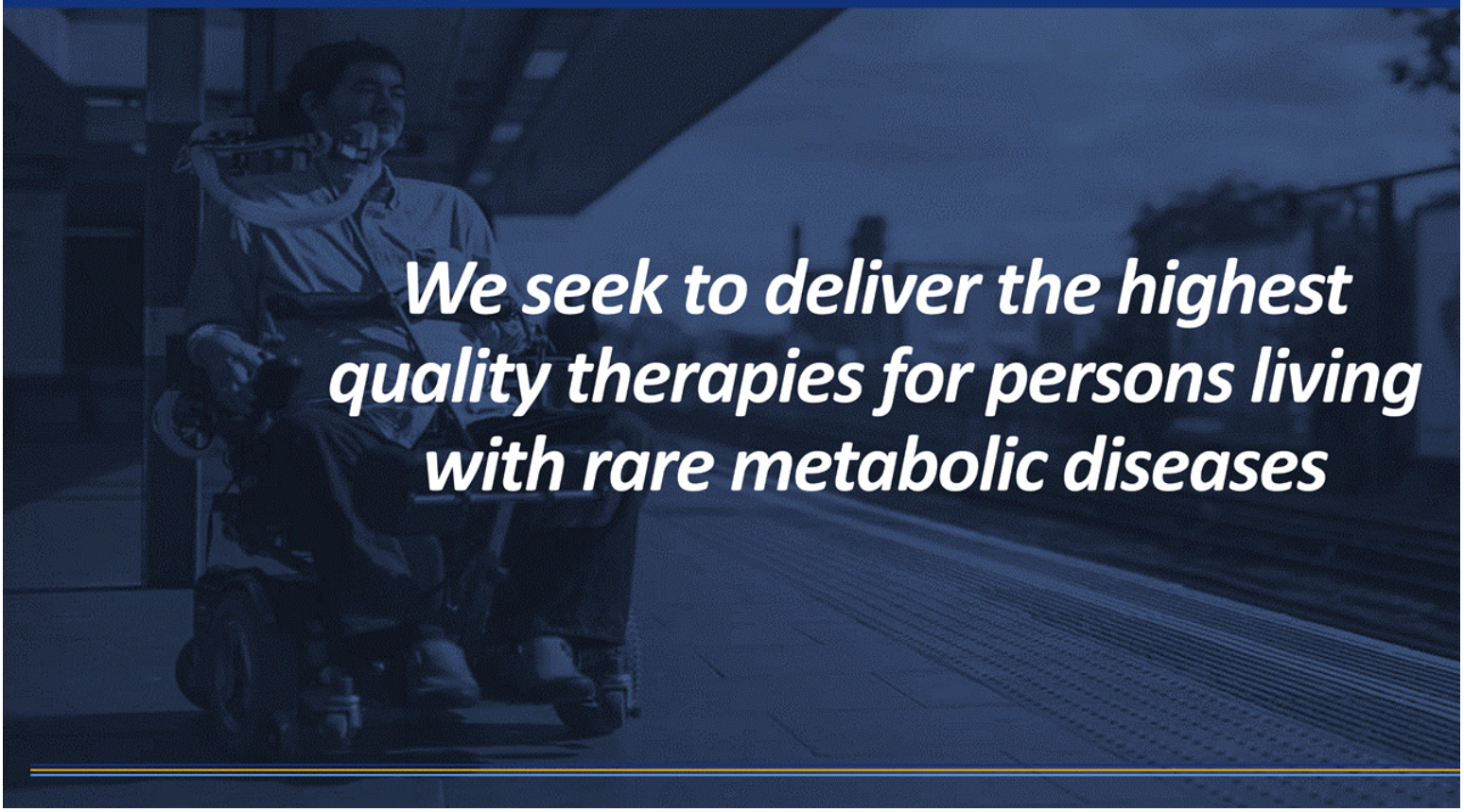
# Amicus Mission






# Amicus Vision: Delivering for Patients and Shareholders

**To build a top-tier, fully integrated, global biotechnology company whose medicines treat 5,000+ patients with $1B+ in worldwide sales revenue by 2023**

**>350 Patients* | $36.9M Global Sales**

**5,000 Patients**

**YE17**

*Clinical & commercial, all figures approximate

# 2018 Key Strategic Priorities

**On Track to Achieve All FIVE Key Strategic 2018 Priorities Outlined in Janu**

1. Double Galafold (migalastat) revenue to $80-$90M
2. ✓ Secure approvals for migalastat in Japan and the U.S.
3. ✓ Achieve clinical, manufacturing and regulatory milestones to advance AT-GAA toward global regulatory submissions and approvals
4. ✓ Develop and expand preclinical pipeline to ensure at least one new clinical program in 2019
5. ✓ Maintain financial strength

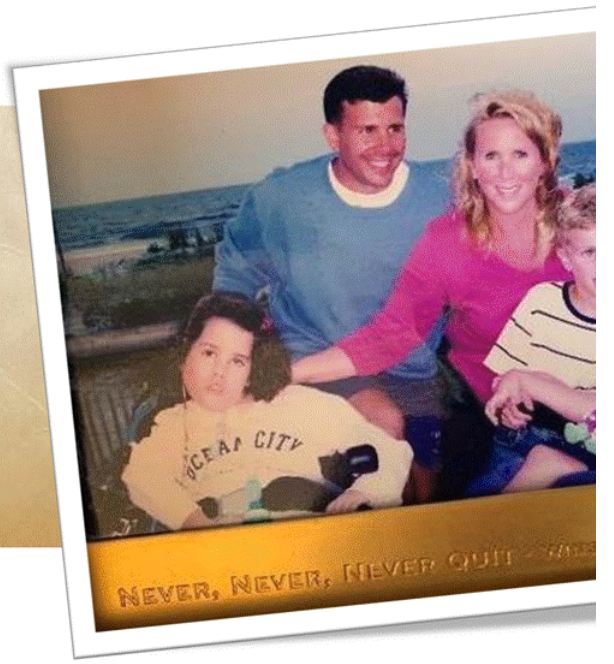
## Integrity Leadership


To achieve our mission for patients and shareholders, we will adhere to the highest levels of business ethics and compliance.

# Persistence

*"Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning."*

*-Winston Churchill*






# Video on Persistence

# Q&A Session

*2018 Analyst Day | October 11, 2018 | Ne*

Thank You