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): **February 5, 2019**

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 February 5, 2019, Amicus Therapeutics, Inc. (the "Company") issued a press release announcing positive data for the Company's Pompe Disease Phase 1/2 Study at the 15th Annual WORLD*Symposium*™. A copy of this press release is attached hereto as Exhibit 99.1. In addition, the Company will be using the presentation attached as Exhibit 99.2 in its meetings with investors and analysts. Both exhibits are incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

Exhibits:

Exhibit No.	Description
99.1	Press release dated February 5, 2019.
99.2	Presentation Materials - "Amicus Data Overview at 15th Annual WorldSymposium™".

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: February 5, 2019

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

Amicus Therapeutics Announces Positive data in Pompe Disease Phase 1/2 Study for Up to 24 Months at 15th Annual WORLD*Symposium*™

Consistent and Durable Responses Across Key Measures of Safety, Functional Outcomes and Biomarkers Continue for both ERT-Naïve and ERT-Switch Patients

Patient Reported Outcomes Data Demonstrate Benefits in Activities of Daily Living and Patient Well Being for AT-GAA Treated Patients

Detailed Positive Data on Non-Ambulatory Patient Cohort Also Highlighted

Webcast for Investors and Analysts on Wednesday, February 6 at 7:00pm ET

CRANBURY, NJ, and Orlando, FL, February 5, 2018 – Amicus Therapeutics (Nasdaq: FOLD) today announced additional positive results from a global Phase 1/2 clinical study (ATB200-02) to investigate AT-GAA in patients with Pompe disease, an inherited lysosomal storage disorder caused by an enzyme deficiency that leads to accumulation of glycogen (disease substrate) in cells. Patients treated with AT-GAA for up to 24 months showed improvements in six-minute walk test (6MWT) distance and other measures of motor function and muscle strength, stability or increases in forced vital capacity (FVC), and durable reductions in biomarkers of muscle damage and disease substrate.

These clinical results, in addition to detailed results on patient-reported outcomes (PROs), are being featured at the 15th Annual World*Symposium*™ in a poster[1] at this afternoon's poster session from 4:30pm to 6:30pm. An additional poster[2] with detailed results for the non-ambulatory cohort in the ATB200-02 study is also part of this afternoon's poster session.

John F. Crowley, Chairman and Chief Executive Officer of Amicus Therapeutics stated, "We are very pleased to report the latest data for AT-GAA, our investigational therapy for Pompe disease, which continues to show very compelling and consistent results across patients and in multiple endpoints now for up to 24 months on treatment. We believe that these longer-term results represent meaningful and very durable improvements in functional outcomes with AT-GAA treatment, in addition to persistent and durable reductions in key biomarkers of muscle damage and disease substrate. These results from the Phase 2 study, together with our ongoing PROPEL pivotal study, support our strategy to advance AT-GAA as quickly as possible with the potential to become the new standard of care for all persons living with Pompe disease."

Mark Roberts, MD, Department of Neurology, Salford Royal NHS Foundation Trust and Principal Investigator in the ATB200-02 study stated, "Patients with Pompe disease are in need of new treatment options that can provide long-term improvement and durability across multiple aspects of their disease. The results from this Phase 1/2 clinical study of AT-GAA continue to demonstrate a robust effect in adult people living with Pompe disease, including meaningful increases in muscle strength in most of the patients, as well as improvements in patient-reported outcomes. Since entering the study, the ambulatory ERT-switch and ERT-naïve participants have walked farther in the 6-minute walking test. Notably, the non-ambulatory ERT-switch participants, a population that is typically excluded from clinical studies, have demonstrated sustained positive changes in their arm and shoulder strength. I look forward to continuing to treat patients in this important clinical study."

ATB200-02 Study Data Highlights in ERT-Switch and ERT-Naive Patients Out to Month 24

The slide deck with the latest clinical results from the ATB200-02 clinical study, in addition to Batten disease preclinical data presented at WORLD*Symposium*, is available at www.amicusrx.com.

Functional Outcomes (n=17): Muscle function improved in 16 out of 17 patients who have available data for up to 21 or 24 months.

- **Motor function:** Six-minute walk test (6MWT) distance, a primary measure of motor function in Pompe disease patients, improved in both ERT-naive and ERT-switch patients with continued benefit observed out to months 21 and 24, respectively. Improvements were generally consistent across both cohorts.
    - All 5 ERT-naive patients showed increases in 6MWT distance at all time points out to month 21. The ERT-naïve patients showed mean increases of 42 meters at month 6 (n=5), 63 meters at month 12 (n=5), and 55 meters at month 21 (n=5).
    - 6MWT increased in 7/10, 9/10, and 8/8 ERT-switch patients at Months 6, 12, and 24 respectively. The ERT-switch patients showed mean increases of 24 meters at month 6 (n=10), 42 meters at month 12 (n=10), and 54 meters at month 24 (n=8).
    - Other motor function tests generally showed mean improvements consistent with 6MWT distance out to month 21 or 24 in both ambulatory cohorts.

- **Muscle Strength:** Non-ambulatory ERT-switch patients showed improvements in upper extremity strength (which includes elbow and shoulder) from baseline to month 21, as measured by quantitative muscle testing (QMT) and manual muscle testing (MMT). Detailed results in this non-ambulatory cohort, who had been on ERT for an average of approximately 10 years, are highlighted in an additional poster[2] today, and a corresponding oral platform presentation on Feb 7, 2019 at 9:15 a.m. ET.

- **Pulmonary Function:** Pulmonary function improved in ERT-naïve patients and was generally stable in ERT-switch patients.
    - In ERT-naïve patients, mean absolute change in forced vital capacity (FVC), one of the main measures of pulmonary function in Pompe disease, was +4.2% at month 6 (n=5), +4.5% at month 12 (n=5), and +6.1% at month 21 (n=5).
    - In ERT-switch patients mean absolute change in FVC was -1.2% at month 6 (n=9), -3.0% at month 12 (n=9), and -0.6% at month 24 (n=7).
    - Overall, other pulmonary tests of maximal inspiratory pressure (MIP), a measure of inhalation, and maximal expiratory pressure (MEP), a measure of exhalation, were stable or increased in both ERT-naïve and ERT-switch patients.

Patient-Reported Outcomes

An interim analysis of patient-reported outcomes from the ATB200-02 clinical study show the benefits in activities of daily living and patient well-being in patients with Pompe disease treated with AT-GAA. Details on these PROs are featured in the poster[1] and will be highlighted in a oral platform presentation on Feb 7, 2019 at 2:00 pm ET.

Safety and Tolerability & Pharmacokinetics/Pharmacodynamics (PK/PD)

- Safety and tolerability data reflect a maximum of 33+ months of treatment. To date, adverse events have been generally mild and transient.
- AT-GAA has resulted in a low rate of infusion-associated reactions (IARs) following 1,110+ infusions (16 incidents of IARs in 6 patients; <1.5% of all 1,110+ infusions with an IAR). The clinical pharmacokinetic profile has been consistent with previously reported preclinical data.
- Persistent and durable reductions in key biomarkers of muscle damage (creatine kinase, or CK) and disease substrate (urine hexose tetrasaccharide, or Hex4) across all patient cohorts out to month 21/24 continue to suggest a positive effect on muscle tissue. Further details are provided in the slide deck.

Patient Disposition

A total of 25 patients have enrolled in the ATB200-02 clinical study across four cohorts. The initial three study cohorts enrolled 22 patients, including ERT-switch ambulatory patients (n=11), ERT-switch non-ambulatory patients (n=6), and ERT-naïve patients (n=5). A fourth cohort of additional ERT-switch ambulatory patients was added to the study and the first three patients' data are available in the most recent interim safety analysis.

	ERT-Switch Cohort 1 (n=11)	Non-Ambulatory ERT-Switch Cohort 2 (n=6)	ERT-Naïve Cohort 3 (n=5)	ERT-Switch Cohort 4 (n=3)[c]	Total
Efficacy	8[a]	4[b]	5	-	17
Safety	11	6	5	3	25

[a]Cohort 1: one patient discontinued after 18 weeks due to travel burden; another patient discontinued due to withdrawal of consent. At the time of this interim analysis, one patient had not reached Month 24.
[b]Cohort 2: one patient discontinued due to IAR. At the time of this interim analysis one patient had not yet reached the initial efficacy assessments (6-month visit).
[c]Cohort 4: currently enrolling ambulatory ERT-switch patients with 7+ years experience with ERT; three patients included in safety database at the time of the interim analysis, none had reached the efficacy assessments (6-month visit)

AT-GAA Development and Regulatory Strategy
The Company's strategy is to enhance the body of clinical data for AT-GAA in ongoing clinical studies, including the pivotal study (PROPEL, also referred to as ATB200-03) to deliver this potential new therapy to as many people living with Pompe disease as soon as possible. Based on regulatory feedback from both the U.S. FDA and European Medicines Agency (EMA), the Company expects the PROPEL study to support approval for a broad indication, including ERT-switch and treatment-naïve patients.

Anticipated 2019 Pompe Milestones:

- Initial 6-month data in additional ERT-switch patients in the Phase 1/2 ATB200-02 clinical study (Cohort 4).
- Retrospective natural history study data in approximately 100 ERT-treated Pompe patients.
- Additional supportive studies, including an open-label study in pediatric patients.
- Full enrollment in Phase 3 PROPEL study.
- Advance agreed upon CMC requirements to support BLA.

Investor and Analyst Webcast on February 6, 2019 at 7:00pm ET
Amicus Therapeutics will host an audio webcast and slide presentation tomorrow, February 6, 2019, at 7:00 p.m. ET to discuss the clinical Pompe disease data and preclinical Batten disease data presented at the WORLD*Symposium*. Dr. Mark Roberts, MD, Department of Neurology, Salford Royal NHS Foundation Trust and Principal Investigator in the ATB200-02 study, will highlight the Pompe data. Dr. Jill M. Weimer, PhD, Senior Director, Therapeutic Development at Sanford Research, will present data from preclinical studies in Batten disease conducted at Sanford Research, which are related to the Amicus gene therapy portfolio licensed from Nationwide Children's Hospital (NCH).

Interested participants and investors may access the webcast via the Investors section of the Amicus Therapeutics corporate website at http://ir.amicusrx.com. A replay of the webcast will be available shortly following the conclusion of the event and it will be archived for 30 days. Participants are encouraged to go to the website 15 minutes prior to the start of the call to register, download, and install any necessary software.

About ATB200-02 Clinical Study
The primary objectives of the open-label ATB200-02 clinical study are to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of ATB200/AT2221 over an 18-week primary treatment period followed by a long-term extension. Sixteen clinical sites in five countries participated in the ATB200-02 clinical study. The study originally enrolled a total of 20 patients across three patient cohorts: ambulatory ERT-experienced (Cohort 1, n=11), non-ambulatory ERT-experienced (Cohort 2, n=4) and ERT-naïve (Cohort 3, n=5); in addition two more patients were enrolled in cohort 2. A fourth cohort of ambulatory ERT-switch patients is also currently enrolling to add to the patient data in the ambulatory ERT-switch population. Patients in Cohort 1 received escalating doses of ATB200 (5, 10, 20 mg/kg), followed by 3 doses of 20 mg/kg ATB200 plus low dose AT2221, followed by ongoing doses of 20 mg/kg ATB200 plus high dose AT2221. Patients in Cohorts 2, 3, and 4 all receive 20 mg/kg ATB200 plus high dose AT2221.

About AT-GAA
AT-GAA is an investigational therapy that consists of ATB200, a unique recombinant human acid alpha-glucosidase (rhGAA) enzyme with optimized carbohydrate structures, particularly mannose-6 phosphate (M6P), to enhance uptake, co-administered with AT2221, a pharmacological chaperone. In preclinical studies, AT-GAA was associated with increased tissue enzyme levels, reduced glycogen levels in muscle, and improvements in muscle strength. A global Phase 1/2 study (ATB200-02) is ongoing to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics of AT-GAA.

Amicus has also initiated a global Phase 3 clinical study (ATB200-03, or PROPEL) of AT-GAA in adult patients with late onset Pompe disease. PROPEL is a 52-week, double-blind randomized study designed to assess the efficacy, safety and tolerability of AT-GAA compared to the current standard of care, alglucosidase alfa, an enzyme replacement therapy (ERT). More information, including a list of participating sites, is available at www.clinicaltrials.gov: NCT03729362.

About Pompe Disease
Pompe disease is an inherited lysosomal storage disorder caused by deficiency of the enzyme acid alpha-glucosidase (GAA). Reduced or absent levels of GAA leads to accumulation of glycogen in cells, which is believed to result in the clinical manifestations of Pompe disease. The disease can be debilitating, and is characterized by severe muscle weakness that worsens over time. Pompe disease ranges from a rapidly fatal infantile form with significant impacts to heart function to a more slowly progressive, late-onset form primarily affecting skeletal muscle. It is estimated that Pompe disease affects approximately 5,000 to 10,000 people worldwide.

About Amicus Therapeutics
Amicus Therapeutics (Nasdaq: FOLD) is a global, patient-dedicated 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, and follow us on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains "forward- looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements relating to encouraging preliminary data from a global Phase 1/2 study to investigate AT-GAA for the treatment of Pompe and the potential implications on these data for the future advancement and development of AT-GAA. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "confidence," "encouraged," "potential," "plan," "targets," "likely," "may," "will," "would," "should" and "could," and similar expressions or words identify forward-looking statements. The forward looking statements included in this press release are based on management's current expectations and belief's which are subject to a number of risks, uncertainties and factors, including that the preliminary data based on a small patient sample and reported before completion of the study will not be predictive of future results, that results of additional preliminary data or data from the completed study or any future study will not yield results that are consistent with the preliminary data presented, that the Company will be not able to demonstrate the safety and efficacy of AT-GAA, that later study results will not support further development, or even if such later results are favorable, that the Company will not be able to successfully complete the development of, obtain regulatory approval for, or successfully commercialize AT-GAA. In addition, all forward looking statements are subject to the other risks and uncertainties detailed in our Annual Report on Form 10-K for the year ended December 31, 2017 and Quarterly Report on 10-Q for the Quarter ended September 30, 2018. As a consequence, actual results may differ materially from those set forth in this press release. You are cautioned not to place undue reliance on these forward looking statements, which speak only of the date hereof. All forward looking statements are qualified in their entirety by this cautionary statement and we undertake no obligation to revise this press release to reflect events or circumstances after the date hereof.

[1]Kishnani, *et. al.*, **15th Annual WORLDSymposium™, First-in-human study of advanced and targeted acid α-glucosidase (AT-GAA) in patients with Pompe disease: Preliminary functional assessment results from the ATB200-02 trial**

[2]Clemens,, *et. al.*, **15th Annual WORLDSymposium™, Safety and efficacy of advanced and targeted acid α-glucosidase (AT-GAA) in ERTswitch non-ambulatory patients with Pompe disease: Preliminary results from the ATB200-02 trial**

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Amicus Therapeutics®

Amicus Data Overview at 15th Annual WorldSymposium™

February 6, 2019 | Orlando, FL

Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to preclinical and clinical development of our product candidates, the timing and reporting of results from preclinical studies and clinical trials, the prospects and timing of the potential regulatory approval of our product candidates, commercialization plans, manufacturing and supply plans, market potential projections, financing plans, and the projected revenues and cash position for the Company. 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, with respect to statements regarding the goals, progress, timing, and outcomes of discussions with regulatory authorities, and in particular the potential goals, progress, timing, and results of preclinical studies and clinical trials, actual results may differ materially from those set forth in this release due to the risks and uncertainties inherent in our business, including, without limitation: 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 we may not be successful in commercializing Galafold in Europe and other geographies or our other product candidates if and when approved; 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; and the potential that we will need additional funding to complete all of our studies and manufacturing. Further, the results of earlier preclinical studies and/or clinical trials may not be predictive of future results. With respect to statements regarding projections of the Company's revenue and cash position, actual results may differ based on market factors and the Company's ability to execute its operational and budget plans. 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 September 30, 2018 filed November 5, 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 news release to reflect events or circumstances after the date hereof.

Agenda

Introduction	Sara Pellegrino
Opening Remarks	John F. Crowley
Pompe Clinical Data Summary	Dr. Mark Roberts
Batten Disease Preclinical Data Summary	Dr. Jill Weimer
Pompe and Fabry Gene Therapy Approach	Dr. Hung Do
Closing Remarks	John F. Crowley
Q&A	

Pompe Key Takeaways

ATB200-02 Study Data Continue to Suggest Potential for AT-GAA to be an Effective and Well-Tolerated Novel Treatment Regimen

- 6MWT distance improvement maintained in both ERT-switch and ERT-naive patients
  - ERT-switch (n=8): Mean **+53.6** meters from baseline to month 24
  - ERT-naive (n=5): Mean **+54.8** meters from baseline to month 21
- Other motor function tests generally consistent with 6MWT results in both ambulatory cohorts
- Muscle strength increased in all cohorts, including non-ambulatory ERT-switch patients
- Pulmonary function
  - FVC, MIP, and MEP increased in ERT-naïve patients
  - FVC and MIP were generally stable and MEP increased in ERT-switch patients
- Patient Reported Outcomes Data Demonstrate Benefits in Activities of Daily Living and Patient Well Being
- Biomarkers and safety
  - CK and Hex4 levels decreased in all cohorts
  - 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.
Based on interim analysis 7.

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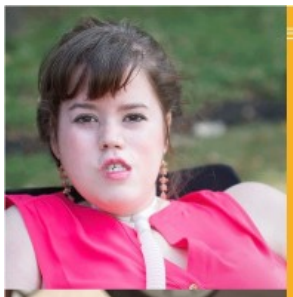


First-in-human Study of ATB200/AT2221 in Patients With Pompe Disease: 24 Month Safety and Efficacy Data From the ATB200-02 Trial

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] Peter Schwenkreis,[10] Kumaraswamy Sivakumar,[11] Ans T. van der Ploeg,[12] Mark Roberts[13]

[1]Klinikum der Universität München-Neurologische Klinik, Friedrich-Baur-Institut, Munich, Germany; [2]PARC Research Clinic, Royal Adelaide Hospital, Adelaide, SA, Australia; [3]University of Florida, Gainesville, FL, USA; [4]University of Pittsburgh and Department of Veterans Affairs Medical Center, Pittsburgh, PA, USA; [5]University Hospital Birmingham NHS Foundation Trust, Queen Elizabeth Medical Center, Birmingham, UK; [6]O&O Alpan LLC, Fairfax, VA, USA; [7]Duke University Medical Center, Durham, NC, USA; [8]Rutgers New Jersey Medical School, Newark, NJ, USA; [9]University of California, Irvine, Orange, CA, USA; [10]Neurologische Klinik und Poliklinik des Berufsgenossenschaftlichen, Universitätsklinikum Bergmannsheil, Bochum, Germany; [11]Neuromuscular Research Center, Phoenix, AZ, USA; [12]Salford Royal NHS Foundation Trust, Salford, UK;

WORLDSymposium | February 6, 2019 | Orlando, FL

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 presentation:

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

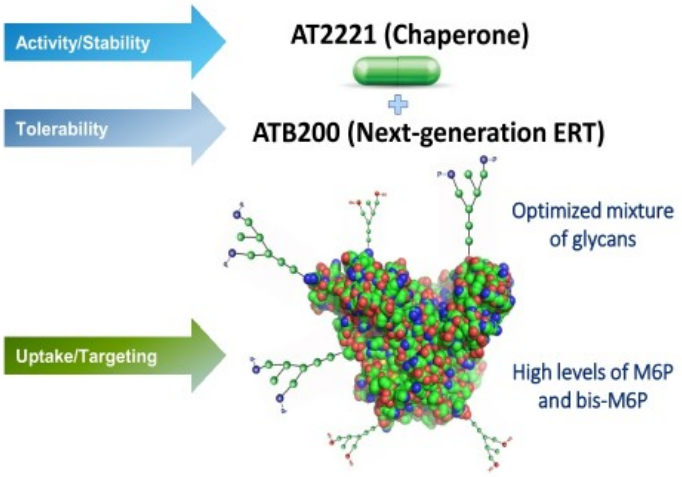
Pompe Disease Overview

- 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 Pompe ERT sales in FY17[2]

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

ATB200 Co-administration With AT2221

- AT-GAA: in development as a novel treatment paradigm that combines 2 investigational agents[1,2]
  - AT2221: orally administered investigational chaperone given 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.

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 Diego, CA, USA.

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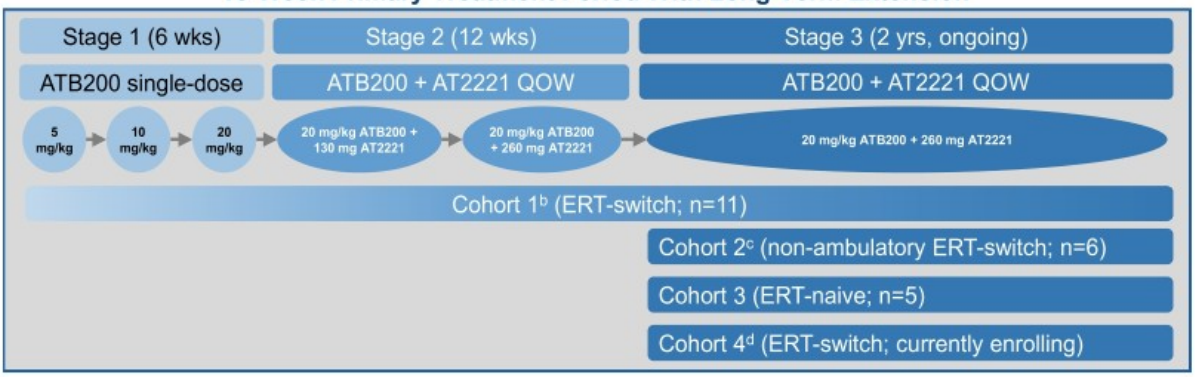
ATB200-02 Study Design (NCT02675465)

in Adults with Late-Onset Pompe Disease (LOPD) in 16 Centers Across 5 Countries

18-Week Primary Treatment Period With Long-Term Extension



- **Assessments:** Safety/tolerability, plasma PK, infusion-associated reactions, antibody levels, PD, efficacy, PRO

LOPD=Late-onset Pompe Disease; PD=pharmacodynamics; PK=pharmacokinetics; PRO=patient-reported outcomes.
[a]Study conducted in 16 centers across 5 countries. [b]2-6 years on ERT; [c]≥7 years on ERT; [d]≥7 years on ERT.

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Baseline Characteristics in Cohorts 1, 2, and 3 (N=22)

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

	Cohort 1 ERT-Switch (N=11[a])	Cohort 2 ERT-Switch Non-ambulatory (N=6[b])	Cohort 3 ERT-Naïve (N=5)
Age, years, mean (min, max)	49.4 (28, 66)	41.5 (18, 57)	49.4 (24, 65)
Sex, M:F	9:2	4:2	1:4
Time on alglucosidase alfa, years, mean (SD)	4.8 (1.42)[a]	10.1 (4.8)	-
6MWT, meters, mean (SD)	392.0 (93.4)	NA	399.5 (83.5)
FVC Upright, % predicted, mean (SD)	52.3 (13.2)	NA	53.4 (20.3)

6MWT=6-minute walk test; ERT=enzyme replacement therapy; FVC=forced vital capacity; LOPD=late-onset Pompe disease; NA=not applicable; SD=standard deviation.
Baseline characteristics not shown for Cohort 4 because efficacy data are not presented for this cohort.
[a]One patient in Cohort 1 discontinued after 18 weeks due to burden of travel; another patient in Cohort 1 withdrew consent. [b]One patient in Cohort 2 discontinued due to an infusion-associated reaction.

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6-Minute Walk Test

6MWT Improved for ERT-Switch Ambulatory and ERT-Naive Patients at Month 6 with Continued Benefit Observed out to Month 24 and 21, Respectively

All results are mean (SD), meter	Baseline	Change From Baseline		
		Month 6	Month 12	Month 24[a,b]
Cohort 1 ERT-Switch Ambulatory	n=10	n=10	n=10	n=8
	397.2 (96.8)	**+23.9** (52.2)	**+42.2** (46.5)	**+53.6** (36.4)
Cohort 3 ERT-Naive	n=5	Month 6 n=5	Month 12 n=5	Month 21 n=5
	399.5 (83.5)	**+41.8** (29.4)	**+63.1** (29.1)	**+54.8** (34.7)

- 6MWT increased in 7/10, 9/10, and 8/8 ERT-switch patients at Months 6, 12, and 24, respectively
- 6MWT increased in 5/5 ERT-naive patients at Months 6, 12, and 21, respectively
- Timed motor function tests were consistent with 6MWT

6MWT=6-minute walk test; ERT=enzyme replacement therapy; SD=standard deviation.
[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.

Amicus Therapeutics

Timed Motor Function Tests

Other Motor Function Tests Generally Consistent with 6MWT; Overall Improvement in Motor Function for Both ERT-switch and ERT-naive Patients over 24 and 21 Months, Respectively

	Test	Baseline, mean (SD)	Change From Baseline, mean (SD)		
			Month 6	Month 12	Month 24
Cohort 1 ERT-Switch Ambulatory		n=10	n=10	n=10	n=8[a,b]
	Timed Up and Go, sec	**10.5** (6.6)	**−1.8** (3.5)	**-1.5** (2.8)	**-1.2** (2.1)
	GSGC Score	**12.6** (4.8)	**+0.1** (3.9)	**-0.3** (4.1)	**-1.6** (2.7)
Cohort 3 ERT-Naive		n=5	Month 6 n=5	Month 12 n=5	Month 21 n=5
	Timed Up and Go, sec	**9.4** (2.3)	**−1.0** (1.1)	**-0.3** (1.9)	**-0.7** (2.4)
	GSGC Score	**12.2** (3.6)	**−1.8** (3.8)	**-0.8** (2.5)	**-1.8** (2.6)

GSGC=Gait, Stairs, Gowers, Chair. GSGC is an observer-rated combined score of 4 motor function assessments: Gait (10m walk), 4-Stair Climb, Gowers (stand from floor), and Rising From Chair. Each test is scored from 1 (normal) to 7 (cannot perform; max score of 6 for Rising From Chair). Total scores range from 4 to 27.

[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.

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Manual Muscle Strength Testing: Cohorts 1, 2 and 3

Consistent and Substantial Increases Observed in Manual Muscle Strengths in All Cohorts Out to Month 21/24; QMT (data not shown) consistent with MMT

	Body Area	Baseline		Change From Baseline					
				Month 6		Month 12		Month 21 or Month 24[a]	
		mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n
ERT-switch Ambulatory	Total Body Max score 80	66.4 (8.1)	10	+2.5 (3.2)	9[b]	+3.3 (3.4)	9[b]	+2.6 (5.0)	7[cd]
ERT-switch Non-Ambulatory	Upper Body Max score 40	13.5 (10.0)	4[e]	+4.5 (0.7)	2[e,f,g]	+2.7 (2.3)	3[e,f]	+1.3 (4.6)	3[e,f]
ERT-Naive	Total Body Max score 80	66.9 (3.7)	5	+0.3 (2.8)	5	+1.1 (3.1)	5	+0.2 (4.4)	5

[a]Month 24 data shown for Cohort 1; Month 21 data shown for Cohort 2 and Cohort 3. [b] One patient missing MMT data at M6 and M12; one patient discontinued prior to month 24 [d]At the time of this interim analysis, 1 patient in Cohort 1 had not reached Month 24. [e] Baseline values missing for 1 patient. [F] One patient discontinued prior to Month 6 assessments. [g]One patient did not complete Month 6 assessment. MMT Scoring: 1) Visible muscle movement, but no movement at the joint; 2) Movement at the joint, but not against gravity; 3) Movement against gravity, but not against added resistance; 4) Movement against resistance, but less than normal; 5) Normal strength.

MMT scoring is the total for left and right sides combined.

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Sitting Forced Vital Capacity (FVC, % Predicted)

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

	Baseline, mean (SD)	Change From Baseline, mean (SD)		
		Month 6	Month 12	Month 24
Cohort 1 ERT-Switch Ambulatory	n=9[a]	n=9[a]	n=9[a]	n=7[abc]
	52.5 (14.8)	**−1.2** (3.9)	**−3.0** (6.0)	**−0.6** (2.8)
Cohort 3 ERT-Naive	n=5	Month 6 n=5	Month 12 n=5	Month 21 n=5
	53.4 (20.4)	**+4.2** (5.6)	**+4.5** (8.4)	**+6.1** (9.7)

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

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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, mean (SD)		
			Month 6	Month 12	Month 24
Cohort 1 ERT-Switch Ambulatory		n=10	n=10	n=10	n=8[ab]
	MIP	**35.7** (11.0)	**+0.3** (4.6)	**0.0** (3.2)	**−1.0** (5.3)
	MEP	**82.7** (26.5)	**+6.0** (24.9)	**+18.5** (33.6)	**+26.5** (32.5)
Cohort 3 ERT-Naive		n=5	Month 6 n=5	Month 12 n=5	Month 21 n=5
	MIP	**32.6** (18.5)	**+11.0** (5.0)	**+5.2** (12.2)	**+7.2** (10.3)
	MEP	**60.6** (8.3)	**−0.4** (12.4)	**+8.6** (16.3)	**+12.4** (20.8)

MEP=maximal expiratory pressure; MIP=maximal inspiratory pressure.
[a]At the time of this interim analysis, 1 patient in Cohort 1 had not reached Month 24. [b]One patient discontinued prior to Month 24
MIP and MEP were measured in cm water.

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Patient-reported outcome instruments

Assessment	Definition	Better functioning/ improvement
Rasch-built Pompe-specific Activity (R-PAct)	18-item questionnaire to measure limitations in activities and social participation in patients with Pompe disease; each activity is ranked from 0 (no) to 2 (yes, without difficulty); total scores range from 0 to 36[1]	 **Higher scores = Less limitations**
Rotterdam Handicap Scale	9-item questionnaire to measure functional ability and level of handicap; each item is ranked from 1 (unable to perform task) to 4 (able to perform task independently); total scores range from 9 to 36[2]	 **Higher scores = Better functioning**
Fatigue Severity Scale (FSS)	9-item questionnaire to measure the severity of fatigue; each question is scored on a scale from 1 (completely disagree) to 7 (completely agree); total scores range from 9 to 63[3]	 **Lower scores = Less fatigue**
Subject Global Impression of Change (SGIC)	Questionnaire to assess the effects of a drug on 8 areas of a patient's life; each question is scored on a scale from 1 (very much worse) to 7 (very much improved)	 **Higher scores = Much improved**

1. Van der Beek NAME et al. *Neuromuscular Disorders*. 2013;23:256-264. 2. Merkies ISJ et al. *Muscle & Nerve*. 2002;25:370-377. 3. Grace J et al. *Parkinsonism Relat Disord*. 2007;13(7):442-445.

R-Pact Improvements

Improvements in activities of daily living (R-Pact) were observed in all cohorts

Max score=36	Baseline		Change From Baseline					
			Month 6		Month 12		Month 24[a]	
	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n
Cohort 1 ERT-Switch	**20.3** (3.6)	10	**+1.5** (3.0)	10	**+1.7** (3.7)	10	**+1.4** (2.5)	8[b,c]
			Month 6		Month 12		Month 21[a]	
Cohort 2 ERT-Switch Non-ambulatory	**1.0** (1.2)	5[d]	**+1.5** (2.4)	4[e]	**+1.0** (2.0)	4	**+1.5** (3.0)	4
Cohort 3 ERT-Naive	**23.6** (4.3)	5	**-0.2** (0.8)	5	**+2.6** (3.5)	5	**+1.8** (2.5)	5

ERT=enzyme replacement therapy; NA=not applicable; SD=standard deviation.

1. Merkies ISJ et al. *Muscle & Nerve*. 2002;25:370-377.

[a]Month 24 data shown for Cohort 1; Month 21 data shown for Cohort 2 and Cohort 3. [b]At the time of this interim analysis, 1 patient in Cohort 1 had not reached Month 24. [c]One patient in Cohort 1 discontinued from study before Month 24. [d]One patient has not reached Month 6 at time of interim analysis and is not included in baseline [e]One patient in Cohort 2 discontinued prior to Month 6

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Rotterdam Handicap Scale

Improvements in functional ability and level of handicap (Rotterdam Handicap Scale) were observed in non-ambulatory ERT-switch patients and ERT-naïve patients

Max score=36	Baseline		Change From Baseline					
			Month 6		Month 12		Month 24[a]	
	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n
Cohort 1 ERT-Switch	**29.7** (4.6)	10	**-1.1** (1.9)	10	**-0.7** (3.2)	10	**-1.6** (2.5)	8[bc]
			Month 6		Month 12		Month 21[a]	
Cohort 2 ERT-Switch Non-ambulatory	**20.0** (5.7)	5[d]	**+1.5** (5.1)	4[e]	**+0.5** (3.9)	3[f]	**+5.6** (7.0)	3[f]
Cohort 3 ERT-Naive	**32.3** (1.8)	5	**-0.5** (1.8)	5	**+0.4** (1.2)	5	**+0.1** (1.2)	5

ERT=enzyme replacement therapy; NA=not applicable; SD=standard deviation.

1. Merkies ISJ et al. *Muscle & Nerve*. 2002;25:370-377. Rotterdam Handicap Scale is a 9-item questionnaire to measure functional ability and level of handicap; each item is ranked from 1 (unable to perform task) to 4 (able to perform task independently); total scores range from 9 to 36; lower scores represent worse functioning.[1]

Data from interim analysis 7.

[a]Month 24 data shown for Cohort 1; Month 21 data shown for Cohort 2 and Cohort 3. [b]At the time of this interim analysis, 1 patient in Cohort 1 had not reached Month 24. [c]One patient in Cohort 1 discontinued from study before Month 24. [d]One patient has not reached Month 6 at time of interim analysis and is not included in baseline [e]One patient in Cohort 2 discontinued prior to Month 6. [f] One patient did not complete questionnaire at Months 12 and 21

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Fatigue Severity Scale

All cohorts were significantly impacted by fatigue at baseline and demonstrated improvements in fatigue over time

Max score=63	Baseline		Change From Baseline					
			Month 6		Month 12		Month 24[a]	
	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n
Cohort 1 ERT-Switch	**53.5** (7.7)	10	**-8.0** (10.7)	10	**-8.0** (6.5)	10	**-4.4** (9.2)	8[bc]
			Month 6		Month 12		Month 21[a]	
Cohort 2 ERT-Switch Non-ambulatory	**44.4** (13.5)	5[d]	**+2.3** (8.7)	4[e]	**-12.5** (10.0)	4	**-15.0** (8.4)	4
Cohort 3 ERT-Naive	**39.2** (12.7)	5	**-5.2** (11.7)	5	**-7.2** (7.5)	5	**-4.6** (8.4)	5

ERT=enzyme replacement therapy; NA=not applicable; 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 fatigue due to the disease condition. The normative value in the healthy population is ~27.[1] Data from interim analysis 7.

[a]Month 24 data shown for Cohort 1; Month 21 data shown for Cohort 2 and Cohort 3. [b]At the time of this interim analysis, 1 patient in Cohort 1 had not reached Month 24. [c]One patient in Cohort 1 discontinued from study before Month 24. [d]One patient has not reached Month 6 at time of interim analysis and is not included in baseline [e]One patient in Cohort 2 discontinued prior to Month 6.

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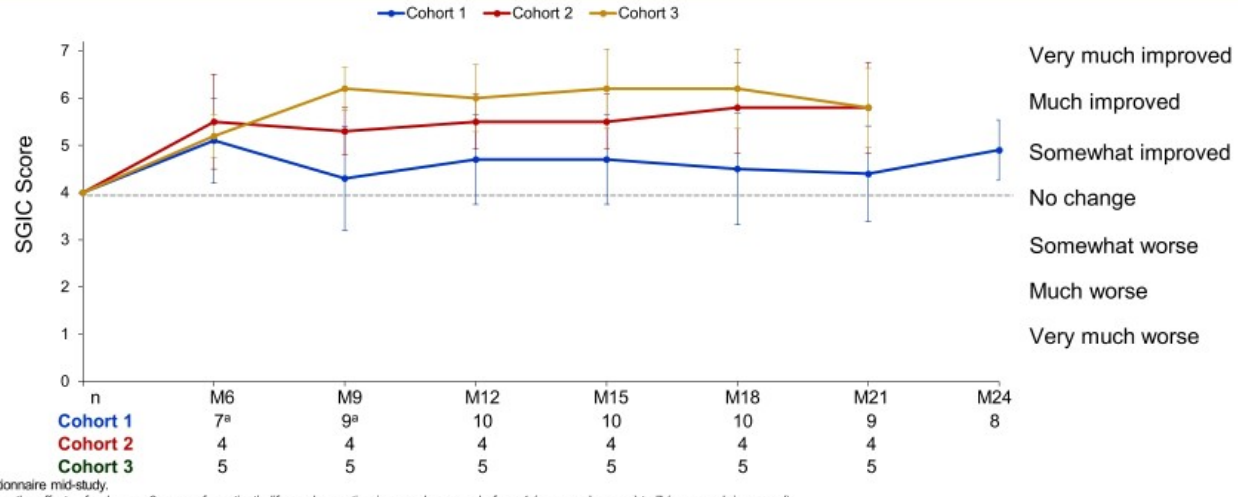
Subject Global Impression of Change: Overall Physical Well-being

Improvements in Physical Well-Being were reported as early as month 6 and were maintained out to month 24



n	M6	M9	M12	M15	M18	M21	M24
Cohort 1	7[a]	9[a]	10	10	10	9	8
Cohort 2	4	4	4	4	4	4	
Cohort 3	5	5	5	5	5	5	

[a]Missing due to change in questionnaire mid-study.
SGIC is a questionnaire to assess the effects of a drug on 8 areas of a patient's life; each question is scored on a scale from 1 (very much worse) to 7 (very much improved).
Mean (SD) scores from overall physical well-being component of the SGIC questionnaire are shown.
Data from interim analysis 7.

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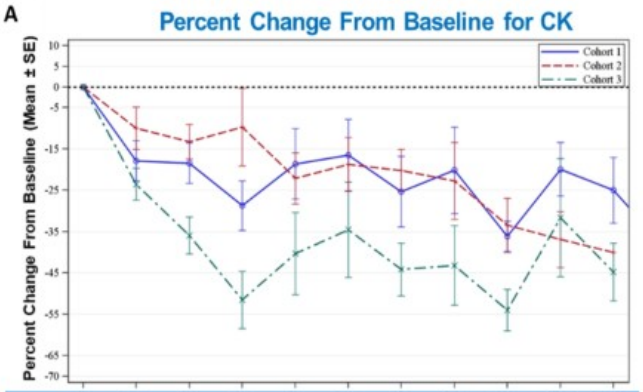
CK and Hex4 Biomarkers

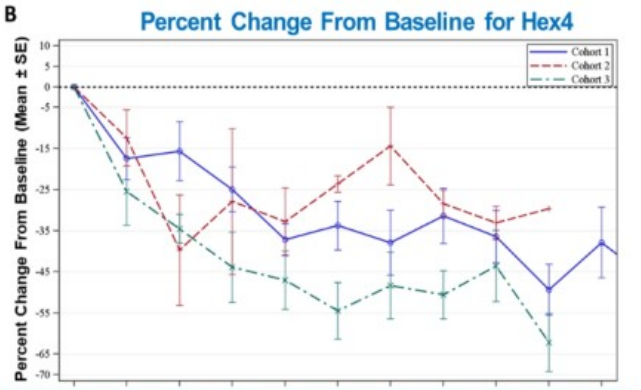
All Cohorts Demonstrated Persistent Improvement in Biomarkers of Muscle Damage (CK) and Disease Substrate (Hex4) For Up To 24 Months

A



n	BL	W2	W4	M3	M6	M9	M12	M15	M18	M21	M24
Cohort 1	11	11	11	11	10	10	10	9	9	7	7
Cohort 2	5	5	5	3	4	4	4	4	4	4	1
Cohort 3	5	5	4	5	5	5	5	3	5	5	2

B



n	BL	W2	W4	M3	M6	M9	M12	M15	M18	M21	M24
Cohort 1	11	11	11	11	10	10	10	10	10	8	7
Cohort 2	6	5	5	5	4	4	4	4	4	1	--
Cohort 3	5	5	5	5	5	5	5	5	5	3	--

BL=baseline; Hex4=urine hexose tetrasaccharide; M=month; SE=standard error; W=week.

Safety Summary (n=25)

Safety data for AT-GAA show AEs have been generally mild and transient with very low rates of IARs (<1.5%) after 1,110+ total infusions across all 4 cohorts

- Safety database includes: 11 Cohort 1 patients, 6 Cohort 2 patients, 5 Cohort 3 patients, 3 Cohort 4 patients*
- Most treatment-emergent AEs were mild or moderate in severity
  - Most common treatment-emergent AEs[a] out of 25 patients: nasopharyngitis (13), fall (10), abdominal pain (9)[b], diarrhea (8), headache (8), upper respiratory tract infection (7), arthralgia (7), nausea (7), back pain (6), fatigue (6), pain in extremities (6), myalgia (6), tremor (5), oropharyngeal pain (5), and muscle spasms (5)
- For serious AEs, 9 events occurred in 5 patients (severity: 2 severe, 5 moderate, 2 mild); 3 events (in 1 patient) were considered probably related to treatment
- One cohort 2 patient discontinued because of a treatment-emergent AE (infusion-associated reaction [IAR]) in cohort 2
- 16 incidents of IARs in 6 patients in 1,110+ infusions
  - 8 IAR events in 5 ERT-switch patients and 8 IAR events in 1 ERT-naive patient
- Longest duration of treatment is 33 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.
Based on interim analysis 7. * 3 patients in Cohort 4 included in safety database at the time of the interim analysis, none had reached the efficacy assessments (6-month visit). Cohort 4 currently enrolling

Conclusions: AT-GAA at up to 24 Months of Treatment

- 6MWT distance improvement maintained in both ERT-switch and ERT-naive patients
  - ERT-switch (cohort 1; n=8): Mean (SD) increase of **+53.6** (36.4) meters from baseline to month 24
  - ERT-naive (cohort 3; n=5): Mean (SD) increase of **+54.8** (34.7) meters from baseline to month 21
- Other motor function tests were generally consistent with 6MWT results in both ambulatory cohorts
- Muscle strength increased in all cohorts, including non-ambulatory ERT-switch patients
- Pulmonary function
  - FVC, MIP, and MEP increased in ERT-naïve patients
  - FVC and MIP were generally stable and MEP increased in ERT-switch patients
- Patients reported improvements in activities of daily living as measured using PROs
- Biomarkers and safety
  - CK and Hex4 levels decreased in all cohorts
  - ATB200/AT2221 was generally well tolerated
- Data from this interim analysis suggest that AT-GAA has the potential to be an effective and well-tolerated novel treatment regimen for patients with LOPD

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.
Based on interim analysis 7.

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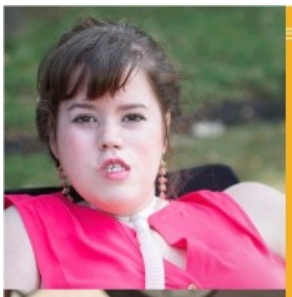

Systematic approach in therapy design reduces pathological and behavioral deficits and prolongs survival in mouse models of CLN3-, CLN6-, and CLN8-Batten disease

Jill Weimer

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[1] Pediatrics and Rare Diseases Group, Sanford Research, Sioux Falls, SD USA; [2] The Research Institute at Nationwide Children's Hospital, Columbus, Ohio, USA; [3]The Mannheimer Foundation, Inc., Homestead, FL, USA; [4]Department of Biochemistry, School of Biomedical Sciences, Brain Health Research Centre, University of Otago, Dunedin, New Zealand; [5]Division of Biology, Kansas State University, Manhattan, KS, USA; [6]AveXis Inc., Bannockburn, IL, USA; [7]Department of Pediatrics, Sanford School of Medicine, University of South Dakota, Sioux Falls SD USA.

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Disclosure Information

I have the following financial relationships to disclose:

- Served as Investigator for the AAV9 mouse studies (in CLN3, CLN6, and CLN8) conducted at Sanford Research and discussed in the presentation

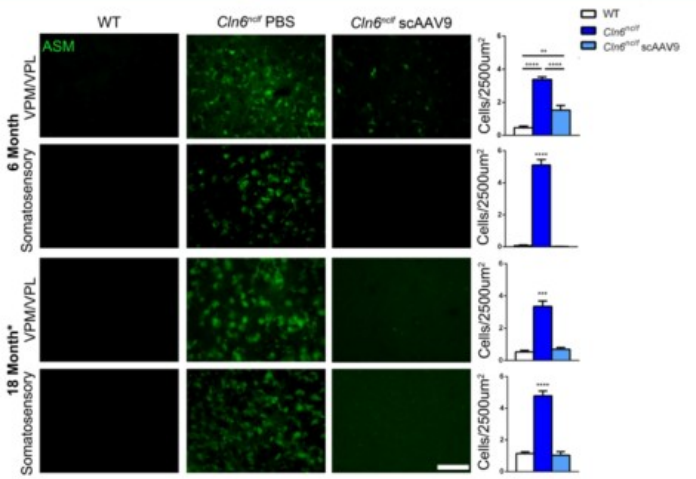
I will discuss the following off-label use and/or investigational use in my presentation:

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

CLN6: Preclinical Mouse Data – Autofluorescent Storage Material

Single AAV9-CLN6 Administration Results in Reduction of Autofluorescent Substrate Material 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

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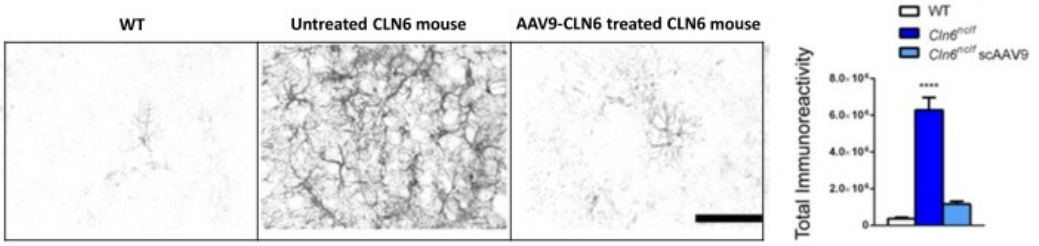
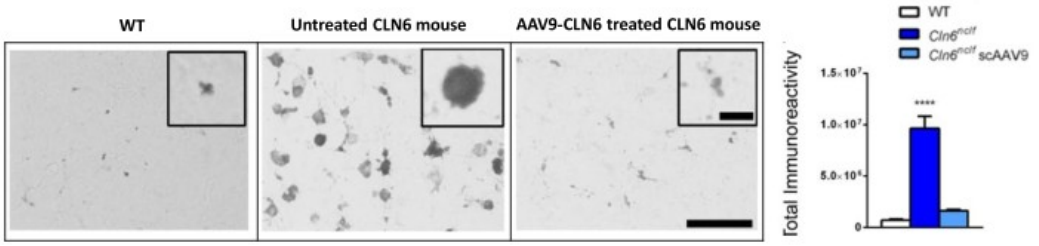
CLN6: Preclinical Mouse Data – Somatosensory Glial Activation

Single AAV9-CLN6 Administration Results in Reduction of Glial Activation

Astrocyte Activation: Month 18



Microglial Activation: Month 18



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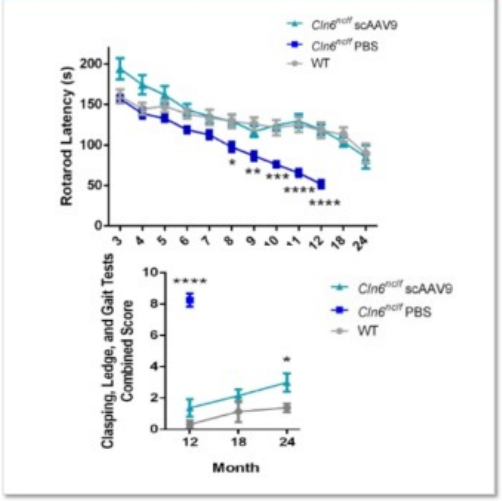
CLN6: Preclinical Mouse Data

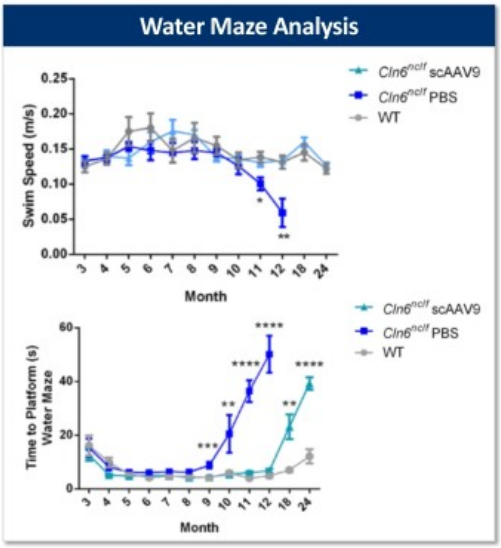
Motor Performance and Cognitive Behavior

Single AAV9-CLN6 Administration Improves Motor Performance & Cognitive Behavior Out to Month 24

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

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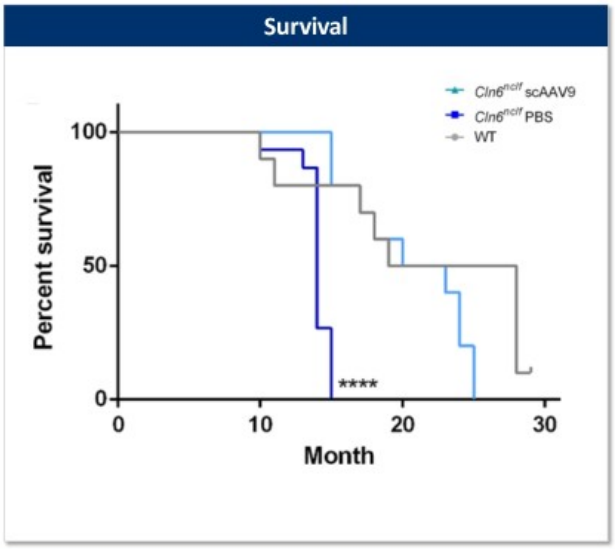
CLN6: Preclinical Mouse Data - Survival

Single AAV9-CLN6 Administration Significantly Extends Median Survival



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

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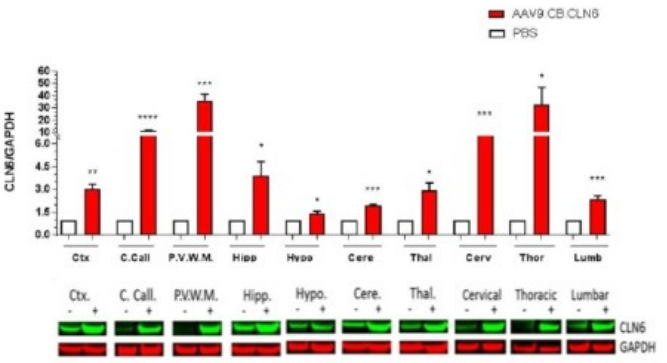
CLN6 Expression in NHP Safety Study

Demonstrated Safety and Meaningful Transduction and CLN6 Expression Throughout the Brain in NHPs

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

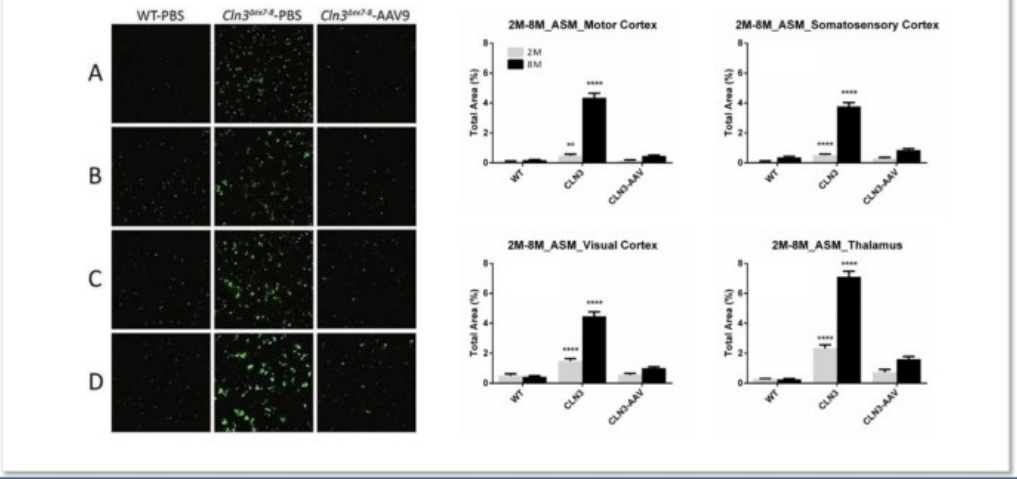
Amicus Therapeutics

Preclinical Proof of Concept Data in CLN3 Batten Disease

CLN3: Preclinical Mouse Data – Autofluorescent Substrate Material

Single AAV9-CLN3 Administration Results in Reduction of Autofluorescent Substrate Material Throughout the Brain

Autofluorescent Storage Material Accumulation



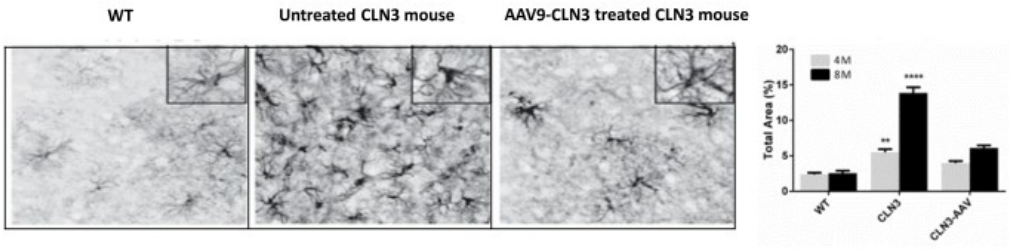
Source: Likhite 2018, 16th International Conference on Neuronal Ceroid Lipofuscinoses, IND-enabling Preclinical Studies for Batten Disease Gene Therapy

Amicus Therapeutics

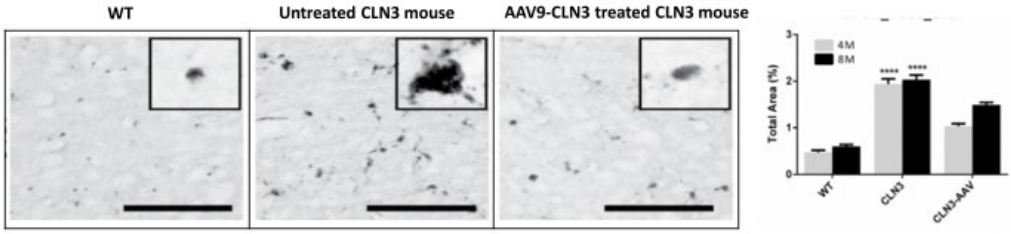
CLN3: Preclinical Mouse Data – Somatosensory Glial Activation

Single AAV9-CLN3 Administration Results in Reduction of Glial Activation

Astrocyte Activation: Month 8



Microglial Activation: Month 8



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

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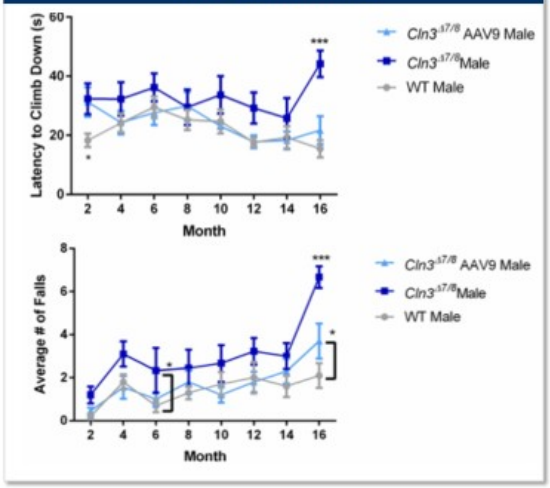
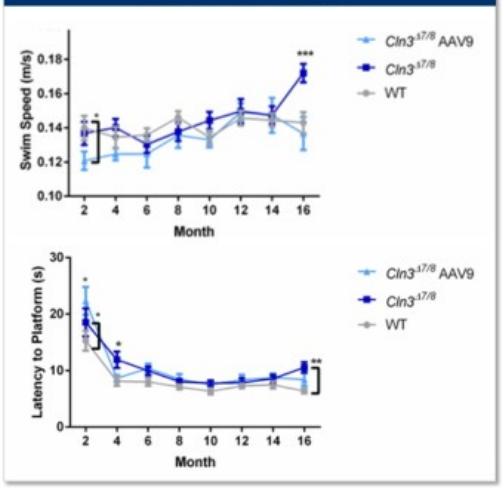
CLN3: Preclinical Mouse Data - Motor Performance & Cognitive Behavior

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

Motor Performance



Water Maze Analysis



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

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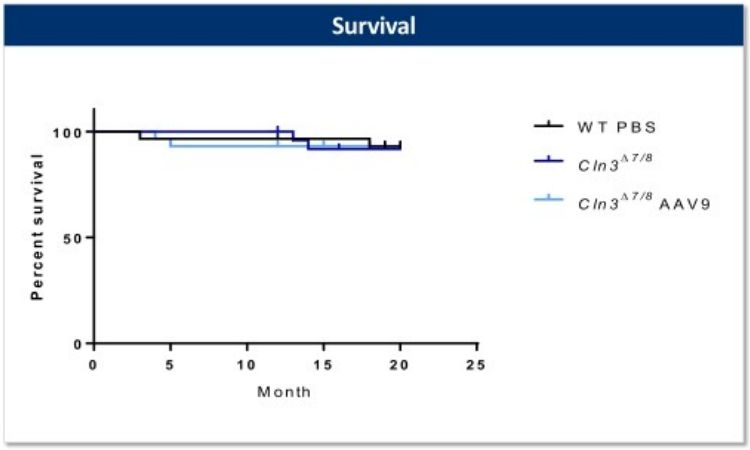
CLN3: Preclinical Mouse Data - Survival

Effect of AAV9-CLN3 On Survival Cannot Yet Be Determined Given Minimal Phenotype in Mouse Model



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

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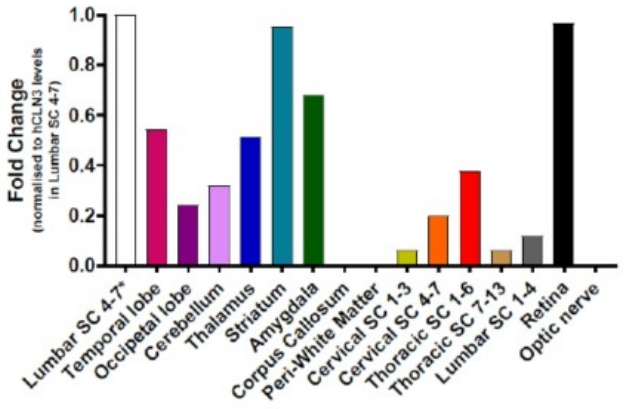
CLN3 Expression in NHP Safety Study

Demonstrated Safety and Meaningful Transduction and Expression Throughout the Brain in NHPs

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

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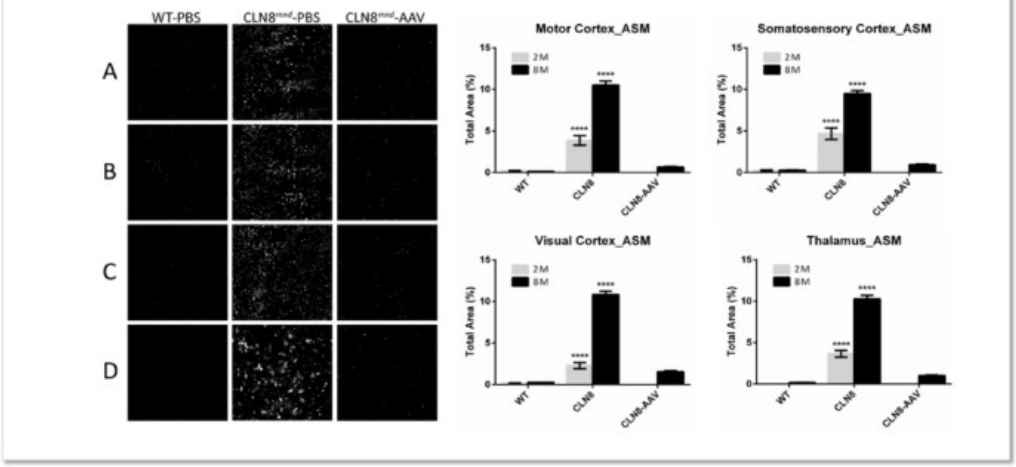
Preclinical Proof of Concept Data in CLN8 Batten Disease

CLN8: Preclinical Mouse Data – Autofluorscent Storage Material

Single AAV9-CLN8 Administration Results in Reduction of Autofluorescent Substrate Material 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

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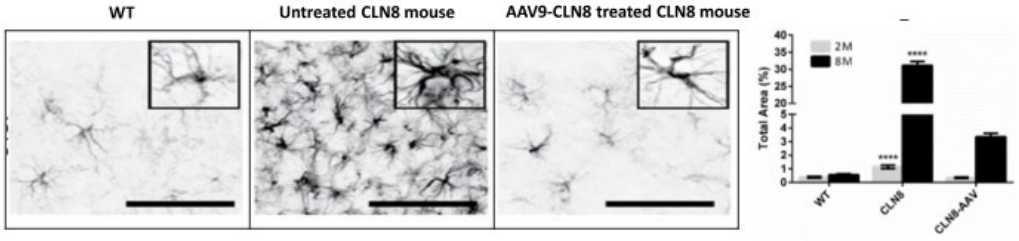
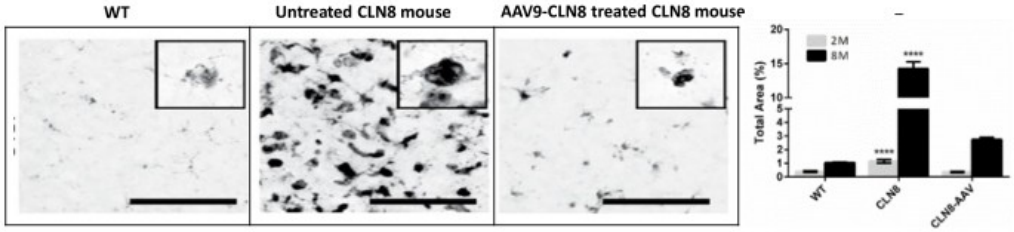
CLN8: Preclinical Mouse Data - Somatosensory Glial Activation

Single AAV9-CLN8 Administration Results in Reduction of Glial Activation

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 Cln8^{mnd} mouse model

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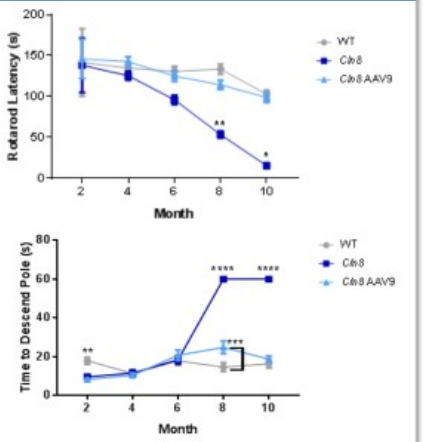
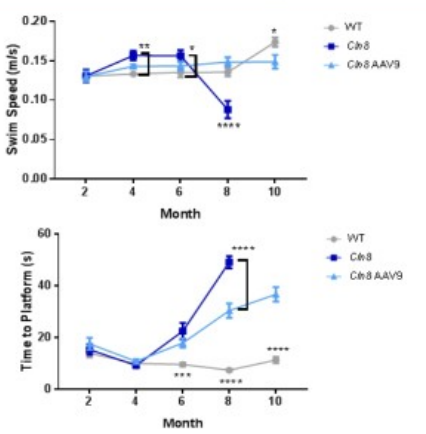
CLN8: Preclinical Mouse Data - Motor Performance and Cognitive Behavior

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

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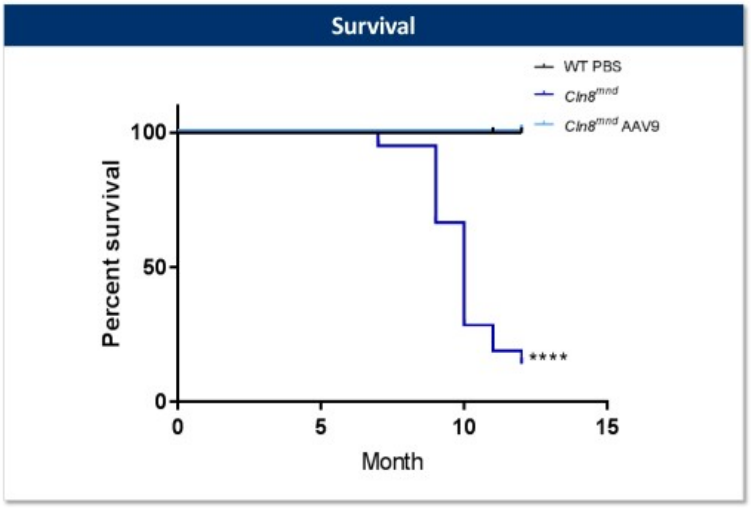
CLN8: Preclinical Mouse Data - Survival

Single AAV9-CLN8 Administration Significantly Extends Median 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

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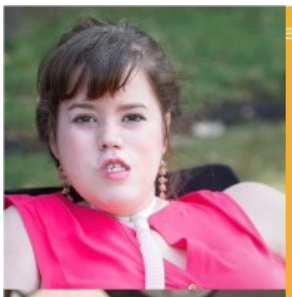


Gene Therapy Pipeline

Hung Do, Chief Science Officer

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

Leading LSD Gene Therapy Portfolio

Amicus is the Consolidator of the Most Promising Gene Therapy Programs in LSDs

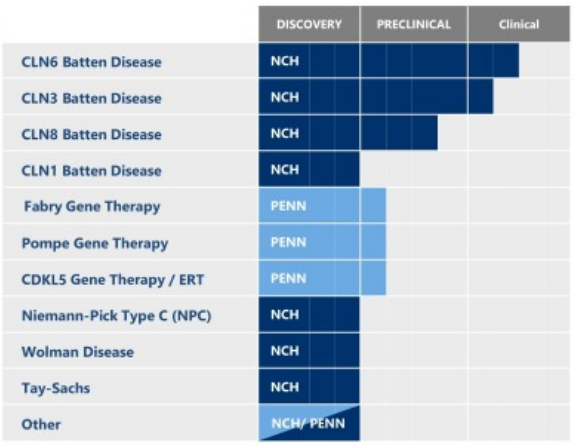
Nationwide Children's

Gene Therapy Program

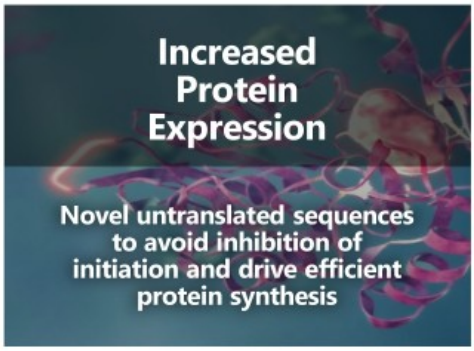
Penn

Amicus Therapeutics

Amicus Gene Therapy Portfolio



Amicus Protein Engineering Expertise & Technologies for Gene Therapy



GENE THERAPY PROGRAM

Penn

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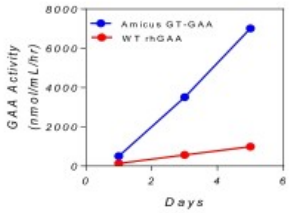
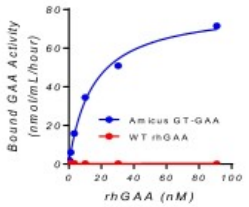
Early Proof of Principle for Optimized Gene Therapy

Pompe

Secreted GAA in Media

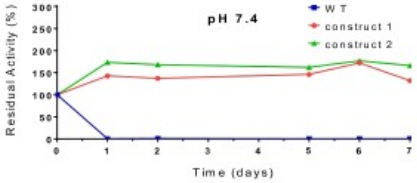


GAA Binding to Intended Receptor

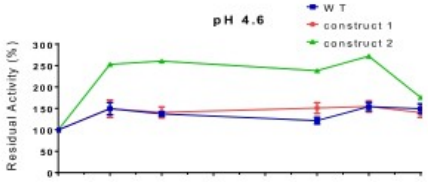


Fabry

Alpha-Gal Activity: pH 7.4



Alpha-Gal Activity: pH 4.6



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Thank You

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