# 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 2, 2019**

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

**Delaware**
(State or Other Jurisdiction of
Incorporation)

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

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

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

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

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

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

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

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

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

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

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

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2). Emerging growth company ☐

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. ☐

**Item 8.01. Other Events**

On October 2, 2019, Amicus Therapeutics, Inc. (the "Company") issued a press release announcing additional positive results from a global Phase 1/2 clinical study (ATB200-02) to investigate AT-GAA in adult patients with Pompe disease. 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 an oral platform presentation on Friday October 4, 2019 at the 24th International Annual Congress of the World Muscle Society. Both exhibits are incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits**

**Exhibits:**

| Exhibit No. | Description |
|---|---|
| 99.1 | October 2, 2019 Press Release |
| 99.2 | Presentation Materials |
| 104 | The cover page from this Current Report on Form 8-K, formatted in Inline XBRL |

**Signature Page**

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: October 2, 2019

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

**Exhibit 99.1**

**Amicus Therapeutics Announces Additional Positive Data in Pompe Disease Phase 1/2 Study of AT-GAA at the 24th International Annual Congress of the World Muscle Society**

***Persistent and Durable Responses Across Safety, Functional Outcomes and Biomarkers for ERT-Naïve and ERT-Switch Patients in Cohorts 1, 2 and 3 Out to Month 24***

***Data in Additional Switch Patients (Cohort 4) Consistent with Reponses in Previous Cohorts Demonstrating Improvements in Multiple Measures of Muscle Function, Pulmonary Function and All Key Biomarkers of Disease***

***Further Evidence of Potential to Positively Change the Course of Disease in Pompe Patients***

**CRANBURY, NJ, and COPENHAGEN, Denmark, October 2, 2019** – Amicus Therapeutics (Nasdaq: FOLD) today announced additional positive results from a global Phase 1/2 clinical study (ATB200-02) to investigate AT-GAA in adult patients with Pompe disease, an inherited lysosomal storage disorder caused by an enzyme deficiency that leads to accumulation of glycogen (disease substrate) in cells. The U.S. Food and Drug Administration (FDA) previously granted Breakthrough Therapy Designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease based on clinical efficacy results this Phase 1/2 clinical study, including improvements in six-minute walk distance in late onset Pompe patients and comparison to natural history of treated patients.

Patients treated with AT-GAA for 24 months showed persistent and durable effects on six-minute walk test (6MWT) distance and other measures of motor function and muscle strength, stability or increases in forced vital capacity (FVC), and reductions in biomarkers of muscle damage and disease substrate. Consistent with these 24-month results, positive impacts on the same measures of motor and pulmonary function and key biomarkers were also observed after 3-15 months of treatment in an additional group of six ambulatory ERT switch patents that had been on standard of care ERT for at least seven years prior to switching to AT-GAA. (Cohort 4).

These clinical results are being featured at the 24th International Annual Congress of the World Muscle Society in an oral platform presentation on Friday October 4, 2019 at 10:00am CEST (4:00am EDT). The presentation will be given by Professor Benedikt Schoser, senior consultant at the Friedrich-Baur-Institute, Dept. of Neurology at the Ludwig-Maximilians-University of Munich, Germany and Principal Investigator in the ATB200-02 study. These results are also available in a presentation on the Amicus corporate website and will be highlighted during the Amicus Analyst Day on October 10, 2019.

John F. Crowley, Chairman and Chief Executive Officer of Amicus Therapeutics stated, "We are very pleased to report the latest data for AT-GAA. Collectively these data continue to represent meaningful and durable improvements in functional outcomes, in addition to persistent reductions in key biomarkers of muscle damage and disease substrate. Compared to what is known about the natural history of both untreated and ERT-experienced patients, these results give great hope that AT-GAA has the potential to become the new standard of care for people living with Pompe. These results also provide further support and confidence in the overall study design and powering of our ongoing pivotal PROPEL study."

Dr. Shoser stated, "There is a clear need for a new treatment option to address multiple aspects of Pompe disease across a broad spectrum of Pompe patients, including previously untreated and ERT-switch patients as well as non-ambulatory patients. The twenty four month 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 improvements in six minute walk distance among ambulatory ERT-switch and ERT-naïve participants and sustained positive changes in arm and shoulder strength among the non-ambulatory ERT-switch patients. These new data in the Cohort 4 patients are particularly impressive showing the potential for AT-GAA to change the course of the disease in these patients. I look forward to continuing to follow patients from this Phase 2 study in addition to the ongoing PROPEL pivotal study."

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

**Cohort 1 – 3 (n=22)**
Complete 24-month data was presented for 18 out of 22 patients enrolled in the initial three study cohorts, including ERT-switch ambulatory patients (n=11), ERT-switch non-ambulatory patients (n=6), and ERT-naïve patients (n=5).

**Functional Outcomes (n=18)*:** Muscle function improved in 16 out of 18 patients at 24 months.

- **Motor function:** Six-minute walk test (6MWT), 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 month 24. Improvements were generally consistent across both cohorts.
  - All 5 ERT-naive patients showed increases in 6MWT distance at all time points out to month 24. The ERT-naïve patients showed mean increases of 42 meters at month 6 (n=5), 63 meters at month 12 (n=5), and 61 meters at month 24 (n=5).
  - 6MWT increased in 7/10, 9/10, and 8/9 ERT-switch patients in Cohort 1 at months 6, 12, and 24 respectively. The ERT-switch patients in Cohort 1 showed mean increases of 24 meters at month 6 (n=10), 42 meters at month 12 (n=10), and 36 meters at month 24 (n=9).
  - Other motor function tests generally showed mean improvements consistent with 6MWT distance out to month 24 in all ambulatory cohorts.

- **Muscle Strength:** Ambulatory and non-ambulatory ERT-switch patients showed improvements in strength testing as assessed by manual muscle testing (MMT) from baseline to month 24. Quantitative muscle testing (QMT) results were generally consistent with MMT.

- **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 +6.8% at month 24 (n=5).
  - In ERT-switch patients in Cohort 1, mean absolute change in FVC was -1.2% at month 6 (n=9), -3.0% at month 12 (n=9), and +0.9% at month 24 (n=8).
  - 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 across all cohorts.

**Cohort 4 (n=6)**
A fourth cohort of six additional ERT-switch ambulatory patients was subsequently added to the study. At the time of the data analysis, five patients have available data at month 6. The last available timepoint includes all six patients after 3-15 months of treatment, with one subject at month 3, two subjects at month 6, two subjects at month 12 and one subject at month 15.

- **Motor Function**: Muscle function improved in 2/5 patients at month 6 and 4/6 patients at the last available time point:
  - Historical data on 6MWT for the six patients showed an average decline of approximately 7 meters per year while on standard of care ERT prior to switching to AT-GAA (n=6), with 5/6 patients declining.
  - After switching to AT-GAA, the patients in Cohort 4 showed mean increases of 24 meters at month 6 (n=5) and 19 meters at their last available timepoint (n=6). 6MWT increased in 2/5 patients at month 6 and 4/6 patients at the last available time point.
  - Other motor function tests generally showed mean improvements consistent with 6MWT distance at month 6 (n=5) and at their last available timepoint (n=6).
  - All patients showed improvements in strength testing from baseline to month 6 and at the last available timepoint, as measured by quantitative muscle testing (QMT) and manual muscle testing (MMT).

- **Pulmonary Function**: Pulmonary function improved at month 6 (n=5) and at the last available time point (n=6).
  - After switching to AT-GAA, FVC increased in 5/6 patients at month 6 and 5/6 patients at the last available time point. Mean absolute change in FVC was +6.6% at month 6 (n=5) and +5.2% at the last available time point (n=6).
  - 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 all patients at month 6 (n=5) and at the last available timepoint (n=6).

**Safety, Tolerability and Pharmacokinetics/Pharmacodynamics (PK/PD) in Cohorts 1-4 (n=28)**

- Safety and tolerability data reflect a maximum of 40 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 1,500+ infusions (28 incidents of IARs in 8 patients; 1.8% of all 1,500+ 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 24 continue to suggest a positive effect on muscle tissue.
- Anti-GAA antibodies were observed in the majority of Cohort 1 and Cohort 3 patients from baseline to month 24. There was no impact of antibodies on safety, efficacy and exposure or clearance of ATB200. Data on impact of antibodies for Cohorts 2 and 4 are not currently available.

**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 feedback from US and EU regulatory authorities, Amicus expects the PROPEL study to support approval for a broad indication, including ERT-switch and treatment-naïve patients.

**Anticipated Pompe Milestones:**

- Presentation of 24-month and Cohort 4 Phase 2 results at Amicus Analyst Day on October 10, 2019.
- Additional supportive studies, including an open-label study in pediatric patients.
- Full enrollment in Phase 3 PROPEL study in 2019.
- Advance agreed upon CMC requirements to support BLA.
- Publication of Phase 1/2 clinical results.

*Discontinuations were as follows: Cohort 1 (n=2 out of 11): travel burden (after 18 weeks), withdrawal of consent (not related to treatment) (after month 18). Cohort 2 (n=1 out of 6): IAR (after month 18 - 4 IARs, generally urticarial rash, with nasopharyngeal edema on 1 occasion. Baseline values not obtained in one patient in Cohort 2. No discontinuations in Cohorts 3 or 4.

**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 6 ambulatory ERT-switch patients was also been enrolled, adding 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 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, 2018 and Quarterly Report on 10-Q for the Quarter ended June 30, 2019. 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.

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FOLD–G

**Exhibit 99.2**

# First-in-Human Study of ATB200/AT2221 in Patients With Pompe Disease: 24-Month Functional Assessment Results From the ATB200-02 Trial

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

[1] Klinikum der Universität München-Neurologische Klinik, Friedrich-Baur-Institut, Munich, Germany; [2]Duke University Medical Center, Durham, NC, USA; [3]PARC Research Clinic, Royal Adelaide Hospital, Adelaide, SA, Australia; [4]University of Florida, Gainesville, FL, USA; [5]University of Pittsburgh and Department of Veterans Affairs Medical Center, Pittsburgh, PA, USA; [6]LDRTC, Fairfax, VA, USA; [7]Rutgers New Jersey Medical School, Newark, NJ, USA; [8]Salford Royal NHS Foundation Trust, Salford, UK; [9]Neurologische Klinik und Poliklinik des Berufsgenossenschaftlichen, Universitätklinikum Bergmannsheil, Bochum, Germany; [10]Neuromuscular Research Center, Phoenix, AZ, USA; [11]Erasmus MC University Medical Center, Rotterdam, Netherlands; [12]Amicus Therapeutics, Inc., Cranbury, NJ, USA; [13]University of California, Irvine, Orange, CA, USA

# Disclosure Statement of Financial Interest

- **Advisory Board:** Audentes Therapeutics, Sanofi-Genzyme, Lupin therapeutics, Nexien Biopharm
- **Speaker's Bureau:** Sanofi Genzyme, Kedrion
- **Research Grant**: Sanofi Genzyme, Greenovation biopharm

# Overview of Pompe Disease

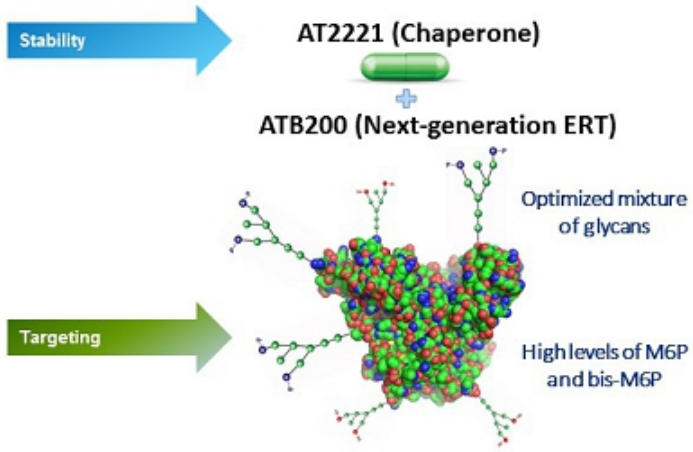
- An inherited lysosomal disorder caused by GAA deficiency[1,2]
- Characterized by progressive accumulation of lysosomal glycogen, primarily in striated muscle[1,2]
- A spectrum of disease severity, including organ failure and/or death[1]
- Can develop at various life stages, from infancy to adulthood[1]
- Skeletal muscle weakness and progressive respiratory involvement are predominant manifestations[1,2]
- Significant unmet medical needs remain despite the enzyme replacement therapy currently available[3]

GAA=acid α-glucosidase; QoL=quality of life.

1. Kishnani PS et al. *Genet Med.* 2006;8(5):267-288. 2. Bijvoet AG et al. *Hum Mol Gen.* 1998;7(1):53-62. 3. Schoser B et al. *BMC Neurology.* 2017;17:202.

# ATB200/AT2221: A Novel Therapy for Pompe Disease

- Novel investigational approach: coadministration of 2 distinct agents
  - ATB200: investigational next-generation ERT
    - Designed with optimized glycosylation and high levels of mannose 6-phosphate residues for better uptake to disease-relevant tissues
  - 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

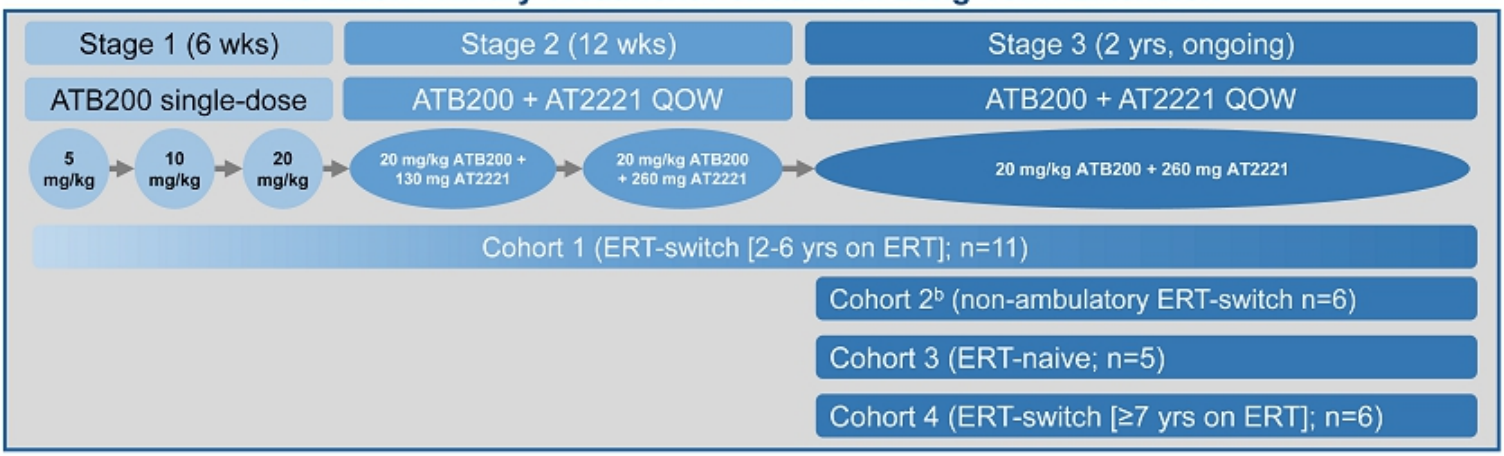



ERT=enzyme replacement therapy; M6P=mannose-6-phosphate.
Xu S, et al. JCI Insight. 2019;4(5):e125358. https://doi.org/10.1172/jci.insight.125358.

# ATB200-02 Study Design (NCT02675465)

- Phase 1/2 study to evaluate safety, tolerability, PK, PD, and efficacy of ATB200/AT2221 in adults with Pompe disease[a]

**18-Week Primary Treatment Period With Long-Term Extension**




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

ERT=enzyme replacement therapy; PD=pharmacodynamics; PK=pharmacokinetics; PRO=patient-reported outcomes; wks=weeks; yrs=years.
[a]Study conducted in 16 centers across 5 countries. [b]≥2 years on ERT.

# Baseline Characteristics

**Patients (N=28) enrolled across cohorts 1, 2, 3 and 4 were representative of the Pompe disease population, with significant impairment at baseline**

| | Cohort 1 ERT-Switch (2-6 yrs on ERT) n=11 | Cohort 2 ERT-Switch[a] Non-ambulatory n=6 | Cohort 3 ERT-Naïve n=5 | Cohort 4 ERT-Switch (≥7 yrs on ERT) n=6 |
|---|---|---|---|---|
| **Age, years, mean (min, max)** | **49.4** (28, 66) | **41.5** (18, 57) | **49.4** (24, 65) | **40.8** (20, 65) |
| **Sex, M:F** | **9:2** | **4:2** | **1:4** | **2:4** |
| **Time on alglucosidase alfa, years, mean (SD)** | **4.8** (1.4) | **10.1** (4.8) | NA | **10.0** (1.6) |
| **6MWT, meters, mean (SD)** | **392.0** (93.4) | NA | **399.5** (83.5) | **387.3 (161.3)** |
| **Upright FVC, % predicted, mean (SD)** | **52.3** (13.2) | 42.3 (28.2)[b] | **53.3** (20.4) | **65.3 (21.1)** |

6MWT=6-minute walk test; ERT=enzyme replacement therapy; FVC=forced vital capacity; NA=not applicable; SD=standard deviation.
[a]Cohort 2 patients were required to have been on alglucosidase alfa for ≥2 years at baseline. [b]n=3.
Data from interim analysis 8.

# 6-Minute Walk Test
## Cohorts 1 and 3

**6MWT improved for both ERT-switch ambulatory and ERT-naive patients at Month 6 with continued benefit observed out to Month 24**

| Cohort | | Baseline (meters) | | Change From Baseline (meters) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Month 6 | | Month 12 | | Month 24 | |
| | | mean (SD) | n | mean (SD) | n | mean (SD) | n | mean (SD) | n |
| 1 | ERT-Switch (2-6 yrs on ERT) | **397.2** (96.8) | 10[a] | **+23.9** (52.2) | 10[a] | **+42.2** (46.5) | 10[a] | **+36.4** (61.7) | 9[ab] |
| 3 | ERT-Naive | **399.5** (83.5) | 5 | **+41.8** (29.4) | 5 | **+63.1** (29.1) | 5 | **+60.7** (36.5) | 5 |

- 6MWT increased in 7/10, 9/10, and 8/9 ERT-switch patients at Months 6, 12, and 24, respectively
- 6MWT increased in 5/5, 5/5, and 5/5 ERT-naive patients at Months 6, 12, and 24, respectively

6MWT=6-Minute Walk Test; ERT=enzyme replacement therapy; SD=standard deviation.
[a]One patient in Cohort 1 discontinued after 18 weeks due to burden of travel; baseline value is not shown for this patient. [b]One patient in Cohort 1 discontinued from study before Month 24.
Data from interim analysis 8.

# Sitting Forced Vital Capacity (FVC, % Predicted)

**On average, FVC remained stable in ERT-switch patients and increased in ERT-naive patients**

| Cohort | | Baseline | | Change From Baseline | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Month 6 | | Month 12 | | Month 24 | |
| | | mean (SD) | n | mean (SD) | N | mean (SD) | n | mean (SD) | n |
| 1 | ERT-Switch (2-6 yrs on ERT) | **52.6** (14.7) | 9[a] | **–1.2** (4.0) | 9[a] | **–3.0** (6.0) | 9[a] | **+0.9** (4.9) | 8[a,b] |
| 3 | ERT-Naive | **53.2** (20.1) | 5 | **+4.4** (5.6) | 5 | **+4.6** (8.8) | 5 | **+6.8** (6.8) | 5 |

- FVC was stable or increased in 5/8 ERT-switch patients at Month 24 (2-6 yrs on ERT); MIP was stable and MEP increased
- FVC was stable or increased in 5/5 ERT-naive patients at Month 24; MIP and MEP both increased

ERT=enzyme replacement therapy; SD=standard deviation.
[a]Baseline FVC not available for 1 patient in Cohort 1. [b]One patient in Cohort 1 discontinued from study before Month 24.
Data from interim analysis 8.

# Manual Muscle Test Score

**Increases were observed in manual muscle strength[a] in Cohorts 1–3 at Month 6 and Month 12, and in Cohorts 1 and 2 at Month 24**

| Cohort | | Body Area | Baseline | | Change From Baseline | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Month 6 | | Month 12 | | Month 24 | |
| | | | mean (SD) | n | mean (SD) | n | mean (SD) | n | mean (SD) | n |
| 1 | ERT switch (2-6 yrs on ERT) | **Total Body** Max score 80 | **66.4** (8.1) | 10[b] | **+2.5** (3.2) | 9[b,c] | **+3.3** (3.4) | 9[b,c] | **+ 3.0** (4.8) | 8[b,c,d] |
| 2 | ERT-switch Non-ambulatory | **Upper Body** Max score 40 | **18.4** (14.0) | 4[e,f] | **+ 2.7** (3.2) | 3[e,f,g] | **+ 2.7** (2.3) | 3[e,f,h] | **+ 3.0** (5.9) | 3[e,f,h] |
| 3 | ERT-Naive | **Total Body** Max score 80 | **66.9** (3.7) | 5 | **+0.3** (2.8) | 5 | **+1.1** (3.1) | 5 | **-1.1** (4.3) | 5 |

- Quantitative muscle strength testing[i] results were generally consistent with manual muscle test results

ERT=enzyme replacement therapy; SD=standard deviation. [a]MMT measured via the Medical Research Criteria (MRC) scale.
[b]One patient in Cohort 1 discontinued after 18 weeks due to burden of travel; [c]One patient missing MMT data at Month 6 and Month 12. [d]One patient in Cohort 1 discontinued prior to Month 24. [e]Baseline value missing for 1 patient. [f]One patient discontinued prior to Month 6 assessments; baseline data are not shown for this patient. [g]Manual muscle testing not completed for one patient. [h]One patient yet to complete Month 12 and 24 [i]Measured via hand-held dynamometer.
Data from interim analysis 8.

# Timed Motor Function Tests

**Timed motor function test results improved for both ERT-switch ambulatory and ERT-naive patients at Month 6 with continued benefit observed out to Month 24**

| Cohort | | Assessment | Baseline, mean (SD) | Change From Baseline, mean (SD) | | |
|---|---|---|---|---|---|---|
| | | | | Month 6 | Month 12 | Month 24 |
| 1 | ERT-Switch (2-6 yrs on ERT) | | n=10[a] | n=10[a] | n=10[a] | n=9[a,b] |
| | | Timed Up and Go, sec | **10.5** (6.6) | **−1.8** (3.5) | **−1.5** (2.8) | **-0.7** (2.5) |
| | | GSGC Score | **12.6** (4.8) | **+0.1** (3.9) | **−0.3** (4.1) | **-0.1** (5.2) |
| 3 | ERT-Naive | | n=5 | n=5 | n=5 | n=5 |
| | | Timed Up and Go, sec | **9.4** (2.3) | **−1.0** (1.1) | **−0.3** (1.9) | **-0.7** (2.0) |
| | | GSGC Score | **12.2** (3.6) | **−1.8** (3.8) | **−0.8** (2.5) | **-1.8** (2.3) |

ERT=enzyme replacement therapy; GSGC=Gait, Stairs, Gowers, Chair; SD=standard deviation.
[a]One patient in Cohort 1 discontinued after 18 weeks due to burden of travel; baseline value is not shown for this patient. [b]One patient in Cohort 1 discontinued from study before Month 24.
GSGC is an observer-rated combined score of 4 motor function assessments: Gait (10-m 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.
Data from interim analysis 8.

# Fatigue Severity Scale
## Patient-Reported Outcome (PRO) Instrument

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

| Cohort Max score=63 | | Baseline | | Change From Baseline | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Month 6 | | Month 12 | | Month 24 | |
| | | mean (SD) | n | mean (SD) | n | mean (SD) | n | mean (SD) | n |
| 1 | ERT-Switch (2-6 yrs on ERT) | **53.5** (7.7) | 10[a] | **-8.0** (10.7) | 10[a] | **-8.0** (6.5) | 10[a] | **-4.1** (8.6) | 9[a,b] |
| 2 | ERT-Switch Non-ambulatory | **45.6** (14.7) | 5[c] | + 2.0 (7.5) | 5[c] | **-12.5** (10.0) | 4[c,d] | **-13.8** (10.9) | 4[c,d] |
| 3 | ERT-Naive | **39.2** (12.7) | 5 | **-5.2** (11.7) | 5 | **-7.2** (7.5) | 5 | **-7.2** (11.9) | 5 |

ERT=enzyme replacement therapy; SD=standard deviation.

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

[a]One patient in Cohort 1 discontinued after 18 weeks due to burden of travel; baseline value is not shown for this patient. [b]One patient in Cohort 1 discontinued from study before Month 24. [c]One patient discontinued prior to Month 6; baseline value was not shown for this patient. [d]one patient did not complete FSS at Months 12 and 24.

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. Lower scores equals less fatigue. The normative value in the healthy population is ~27.[1]

Data from interim analysis 8.

# Clinical Assessments Summary for Cohort 4
## ERT-Switch (≥7 yrs on ERT)

**Improvements seen in majority of the patients both on motor function and strength as well as pulmonary function as assessed by FVC after 3-15 months of treatment**

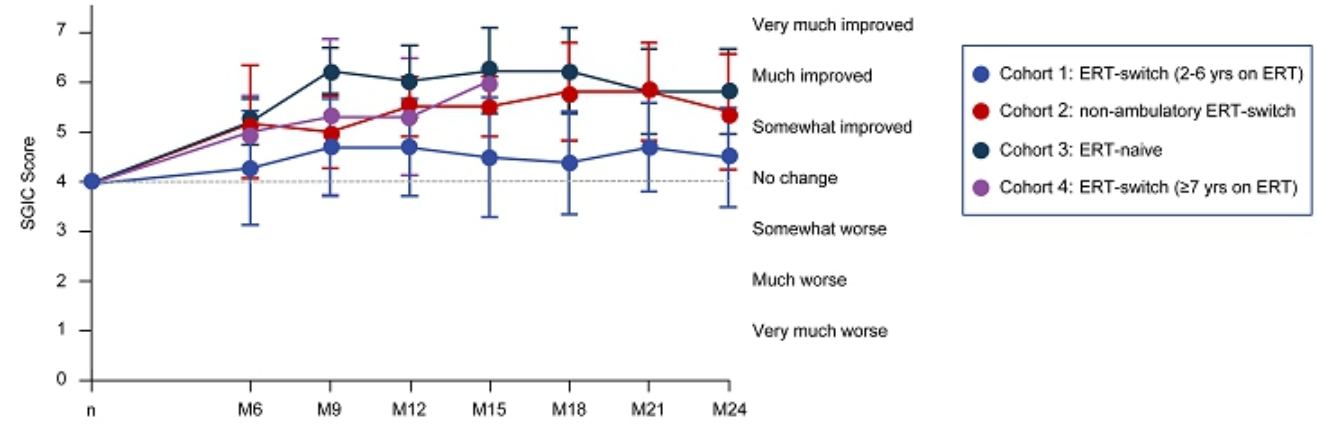
| Cohort 4 | Baseline | | CFBL to 6M | | CFBL to LOCF | |
|---|---|---|---|---|---|---|
| | mean (SD) | n | mean (SD) | n[a] | mean (SD) | n |
| 6MWT, meters | **387.3** (161.3) | 6 | **+24.3** (60.5) | 5 | **+19.3** (53.3) | 6 |
| % predicted sitting FVC | **65.3** (21.1) | 6 | **+6.6** (4.2) | 5 | **+ 5.2** (6.0) | 6 |
| MMT (max 80) | **59.7** (6.0) | 6 | **+ 4.0** (2.0) | 5 | **+ 3.8** (3.8) | 6 |
| Timed up and go, sec | **9.1** (4.2) | 5[b] | 0.3 (1.6) | 5 | **+ 0.6** (1.4) | 5[b] |
| GSGC | **17.2** (5.0) | 6 | **-2.8** (4.0) | 5 | **-2.2** (3.9) | 6 |
| FSS (max 63) | **42.8** (14.0) | 5[b] | **-3.3** (4.6) | 5 | **-3.0** (7.2) | 5[b] |

- 6MWT increased in 2/5 patients at M6 and 4/6 patients at LOCF after 3-15 months of treatment
- FVC increased in 5/5 patients at M6 and 5/6 at LOCF after 3-15 months of treatment; MIP and MEP both increased
- LOCF includes 1 subjects at Month 3, 2 subjects at Month 6, 2 subjects at Month 12 and 1 subject at Month 15

6MWT=6-Minute Walk Test; CFBL=change from baseline; FSS=Fatigue Severity Scale; FVC=forced vital capacity; GSGC=Gait, Stairs, Gowers, Chair; LOCF=last observation carried forward; MMT=manual muscle test. [a]Only 5 patients had completed month 6 assessment at time of IA8. [b]One patient missing data for Timed up and go and one patient missing data for FSS. Data from interim analysis 8.

# Subject Global Impression of Change: Overall Physical Well-being

## Improvements in overall physical well-being in all four cohorts



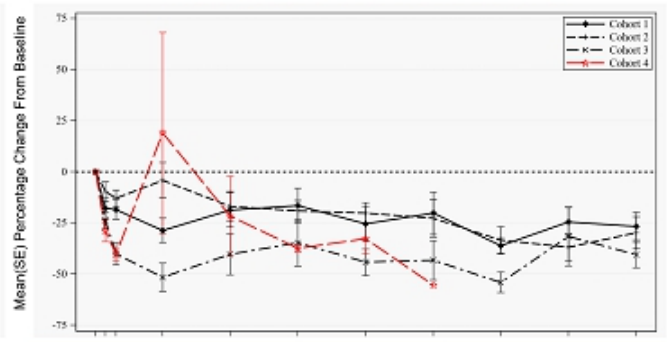

| n | M6 | M9 | M12 | M15 | M18 | M21 | M24 |
|---|---|---|---|---|---|---|---|
| Cohort 1 | 9 | 10 | 10 | 10 | 9 | 9 | 9 |
| Cohort 2 | 5 | 5 | 4 | 4 | 4 | 4 | 5 |
| Cohort 3 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Cohort 4 | 5 | 3 | 3 | 1 | | | |

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 (standard deviation) scores from overall physical well-being component of the SGIC questionnaire are shown. Data from interim analysis 8.

# Muscle damage and disease substrate biomarkers

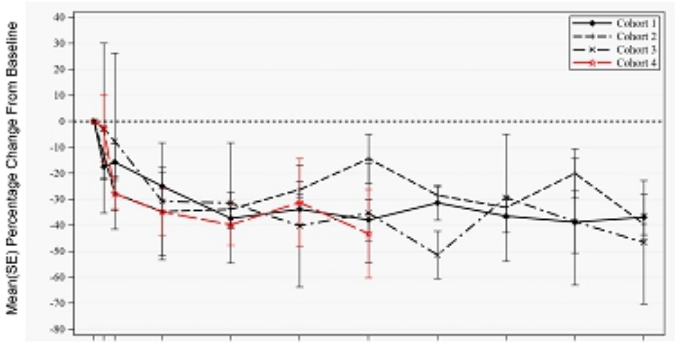
## Persistent improvement in biomarkers of muscle damage (CK) and disease substrate (Hex4) in all cohorts

### Percentage Change From Baseline for CK




| Visit | BL | M3 | M6 | M9 | M12 | M15 | M18 | M21 | M24 |
|---|---|---|---|---|---|---|---|---|---|
| C1 | 11 | 11 | 10 | 10 | 10 | 9 | 9 | 8 | 9 |
| C2 | 5 | 4 | 5 | 5 | 4 | 4 | 4 | 4 | 4 |
| C3 | 6 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 5 |
| C4 | 6 | 6 | 6 | 3 | 3 | 1 | - | - | - |

### Percentage Change From Baseline for Hex4




| Visit | BL | M3 | M6 | M9 | M12 | M15 | M18 | M21 | M24 |
|---|---|---|---|---|---|---|---|---|---|
| C1 | 11 | 11 | 10 | 10 | 10 | 10 | 10 | 9 | 9 |
| C2 | 5 | 5 | 5 | 5 | 4 | 4 | 4 | 3 | 4 |
| C3 | 6 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 5 |
| C4 | 6 | 6 | 5 | 3 | 3 | - | - | - | - |

CK=creatine kinase; Hex4=urine hexose tetrasaccharide; SE=standard error.

# Safety Summary

**Safety data (N=28) for ATB200/AT2221 show that AEs have been generally mild and transient with very low rates of IARs (1.8%) after 1500+ total infusions across all cohorts**

- As of August 28, 2019, the longest treatment duration was 40 months
- Most treatment-emergent AEs were transient and generally mild or moderate in severity
- 11 serious AEs[a] (3 severe, 8 moderate) occurred in 7 patients
  - 6 events, all IARs (in 3 patients) were considered probably related to treatment
- 1 patient discontinued because of a treatment-emergent AE (IAR); a second patient discontinued due to withdrawal of consent
- 28 incidents of IARs (51 events) in 8 patients in 1500+ infusions (1.8% of infusions)
  - 36 IAR events in 7 ERT-switch patients and 15 IAR events in 1 ERT-naive patient (ongoing, 32 months treatment)
- Immunogenicity was observed in the majority of Cohort 1 and Cohort 3 patients up to 24 months

AE=adverse events; ERT=enzyme replacement therapy; IAR, infusion-associated reaction.
[a]Serious adverse events (n events) were: IARs entailing bronchospasm (2), urticaria (1), pharyngeal edema (1), IAR (1); pneumonia (1), lower respiratory tract infection (1), lymphoma (1), syncope (1), diverticulitis (1).

# Conclusions

- Data from this interim analysis show functional benefit of ATB200/AT2221 in patients with Pompe disease out to 24 months for cohorts 1,2 and 3
  - 6MWT and pulmonary function improved with continued benefit observed to Months 24
  - Patients reported decreased fatigue and felt improved as measured using PROs
- Improvements seen in majority of the cohort 4 patients in motor function, muscle strength, and pulmonary function
- Biomarker CK and Hex4 levels decreased in all cohorts
- ATB200/AT2221 was generally well tolerated over 40+ months of treatment
- No impact of immunogenicity on safety, efficacy and exposure or clearance of ATB200
- Phase 3 trial PROPEL (NCT03729362) comparing ATB200/AT2221 with alglucosidase alfa in LOPD is currently underway

6MWT=6-Minute Walk Test; CK=creatine kinase; ERT=enzyme replacement therapy; FVC=forced vital capacity; Hex4=urine hexose tetrasaccharide; LOPD=late-onset Pompe disease; PRO=Patient-Reported Outcome.

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