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 11, 2021**

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.)**

3675 Market Street, Philadelphia, PA 19104
(Address of Principal Executive Offices, and Zip Code)

215-921-7600
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 February 11, 2021, Amicus Therapeutics, Inc. (the "Company") issued a press release announcing topline results of the Company's Phase 3 double-blind randomized study to assess the efficacy and safety of ATB200/AT2221 in adult subjects with late-onset Pompe disease compared with alglucosidase alfa/placebo ("PROPEL"). A copy of this press release is attached hereto as Exhibit 99.1. The Company also released presentation materials they will be using in meetings with investors and analysts. A copy of the presentation materials is attached hereto as Exhibit 99.2. Both exhibits are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits:

Exhibit No.	Description
99.1	Press Release dated February 11, 2021
99.2	February 11, 2021 Presentation Materials
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: February 11, 2021

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

Amicus' AT-GAA Shows Clinically Meaningful & Significant Improvements in Both Musculoskeletal and Respiratory Measures in Late-Onset Pompe Disease Compared to Standard of Care in Pivotal Phase 3 PROPEL Study

Rolling BLA submission for AT-GAA planned for completion in Q2 and other global regulatory submissions for approval expected throughout 2021

Patients switching to AT-GAA from the approved standard of care ERT (alglucosidase alfa) walked on average 17 meters farther (p=0.046)

Patients switching to AT-GAA also showed an improvement in percent-predicted forced vital capacity (FVC), the most important measure of respiratory function in Pompe disease, compared to a decline in patients treated with alglucosidase alfa (FVC Diff. 4.1%; p=0.006)

AT-GAA showed a nominally statistically significant and clinically meaningful difference for superiority on the first key secondary endpoint of FVC compared to patients treated with alglucosidase alfa (FVC Diff. 3.0%; p=0.023)

In the combined study population of ERT switch and ERT naïve patients, AT-GAA outperformed alglucosidase alfa by 14 meters (21m compared to 7m) on the primary endpoint and was not statistically significant for superiority (p=0.072)

Improvements in the two important biomarkers of Pompe disease (Hex-4 and CK) for the combined study population significantly favored AT-GAA compared to alglucosidase alfa (p<0.001)

Conference Call at 4:30pm EST today with results to be presented in a platform presentation session at the 17th Annual WORLDSymposium™ 2021 on Friday, February 12 at 9:30am

Philadelphia, PA, Feb. 11, 2021 (GLOBE NEWSWIRE) -- Amicus Therapeutics (Nasdaq: FOLD), a patient-dedicated global biotechnology company focused on discovering, developing and delivering novel medicines for rare diseases, today announced the topline results of its Phase 3 PROPEL Pivotal Trial for AT-GAA (cipaglucosidase alfa and miglustat), its investigational two-component therapy for the treatment of late-onset Pompe disease (LOPD) that has previously received Breakthrough Therapy Designation from the U.S. FDA and the Promising Innovative Medicine designation from the MHRA in the United Kingdom. With consent from the FDA, the Company initiated a rolling Biologics License Application (BLA) in the fourth quarter of 2020. Amicus plans to complete the BLA submission in the second quarter of this year and anticipates additional regulatory submissions in the European Union and in other geographies throughout 2021.

PROPEL was a 52-week, double-blind randomized global 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). The study enrolled 123 adult Pompe patients who still had the ability to walk and to breathe without mechanical ventilation and was conducted at 62 clinical sites in 24 countries on 5 continents. It was the largest controlled clinical study ever conducted in a lysosomal disorder.

Patients enrolled in PROPEL were randomized 2:1 so that for every two patients randomized to be treated with AT-GAA, one was randomized to be treated with alglucosidase alfa. Of the Pompe patients enrolled in PROPEL, 77% were being treated with alglucosidase alfa (n=95) immediately prior to enrollment and 23% had never been treated with any ERT (n=28). 117 patients completed the PROPEL study and all 117 have voluntarily enrolled in the long-term extension study and are now being treated solely with AT-GAA for their Pompe disease.

“The data for patients treated with AT-GAA in this PROPEL study show clinically meaningful and positive changes in the key manifestations of this disease. Particularly impressive are the clinically significant improvements in musculoskeletal and respiratory endpoints for patients switching from ERT standard of care to AT-GAA. With PROPEL, AT-GAA has proven its high potential to advance the current standard of care for people living with Pompe disease,” stated Prof. Benedikt Schoser, Professor of Neurology at Ludwig-Maximillians-University of Munich LMU Department of Neurology.

“Pompe disease is a devastating neuromuscular disease and patients need new treatment options. Respiratory muscle function is impaired in nearly all Pompe patients and AT-GAA demonstrates for the first time the potential to stabilize breathing in patients who switch from ERT standard of care and this is especially encouraging. These data are compelling for Pompe patients switching to AT-GAA,” according to Dr. Mark Roberts, Consultant Neurologist at the Greater Manchester Neurosciences Unit at Salford Royal NHS Foundation Trust.

“Data from the PROPEL study demonstrate the potential to further improve motor and respiratory functions in patients with Pompe disease. Given the unmet need in this population, the data from the PROPEL study are very encouraging and will provide an important alternative treatment option for patients living with Pompe disease,” stated Dr. Priya Kishnani, Professor of Pediatrics and Chief of Medical Genetics at Duke University School of Medicine.

Pre-Specified Analyses of 6-Minute Walk Distance (6MWD) and Percent-Predicted Forced Vital Capacity (FVC) in the Combined ERT Switch and ERT Naïve Study Population:

The primary endpoint of the study was the mean change in 6-minute walk distance as compared with baseline measurements at 52 weeks across the combined ERT switch and ERT naïve patient populations. In this combined population patients taking AT-GAA (n=85) walked on average 21 meters farther at 52 weeks compared to 7 meters with those treated with alglucosidase alfa (n=37). This primary endpoint in the combined population was assessed for superiority and while numerically greater, statistical significance for superiority on this combined population was not achieved for the AT-GAA arm as compared to the alglucosidase alfa arm (p=0.072).

Per the hierarchy of the statistical analysis plan, the first key secondary endpoint of the study was the mean change in percent-predicted FVC at 52 weeks across the combined population. In this combined population patients taking AT-GAA demonstrated a nominally statistically significant and clinically meaningful difference for superiority over those treated with alglucosidase alfa. AT-GAA significantly slowed the rate of respiratory decline in patients after 52 weeks. Patients treated with AT-GAA showed a 0.9% absolute decline in percent-predicted FVC compared to a 4.0% absolute decline in the alglucosidase alfa arm (p=0.023). Percent-predicted FVC is the most important measure of respiratory muscle function in Pompe disease and was the basis of approval for alglucosidase alfa.

6MWD (m) in the Overall ERT Switch and ERT Naïve Study Population

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=85)	357.9 (111.8)	+20.8 (4.6)	+13.6 (8.3)	p=0.072
Alglucosidase alfa (n=37)	351.0 (121.3)	+7.2 (6.6)		

FVC (% predicted) in the Overall ERT Switch and ERT Naïve Study Population

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=85)	70.7 (19.6)	-0.9 (0.7)	+3.0 (1.2)	p=0.023
Alglucosidase alfa (n=37)	69.7 (21.5)	-4.0 (0.8)		

Pre-Specified Analyses of 6-Minute Walk Distance (6MWD) and Percent-Predicted Forced Vital Capacity (FVC) in the ERT Switch Study Population (n=95):

The PROPEL switch patients entered the study having been treated with alglucosidase alfa for a minimum of two years. More than two thirds (67%+) of those patients had been on ERT treatment for more than five years prior to entering the PROPEL study (mean of 7.4 years).

A pre-specified analysis of the patients switching from alglucosidase alfa on 6-minute walk distance showed that after 52 weeks from switching, AT-GAA treated patients (n=65) walked 16.9 meters farther than their baseline, compared to 0.0 meters for those patients who were randomized to remain on alglucosidase alfa (n=30) (p=0.046).

A pre-specified analysis of the patients switching from alglucosidase alfa on percent-predicted FVC showed that AT-GAA treated patients stabilized and slightly improved their respiratory function on this important measure while those patients remaining on alglucosidase alfa continued to significantly decline in respiratory muscle function. AT-GAA patients showed a 0.1% absolute increase in percent-predicted FVC while the alglucosidase alfa patients showed a 4.0% absolute decline over the course of the year (p=0.006).

6MWD (m) in the ERT Switch Study Population

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=65)	346.9 (110.2)	+16.9 (5.0)	+16.9 (8.8)	p=0.046
Alglucosidase alfa (n=30)	334.6 (114.0)	0.0 (7.2)		

FVC (% predicted) in the ERT Switch Study Population

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=65)	67.9 (19.1)	+0.1 (0.7)	+4.1 (1.2)	p=0.006
Alglucosidase alfa (n=30)	67.5 (21.0)	-4.0 (0.9)		

Pre-Specified Analyses of 6-Minute Walk Distance (6MWD) and Percent-Predicted Forced Vital Capacity (FVC) in the ERT Treatment Naive Population (n=28):

A pre-specified analysis of the patients previously never treated with any ERT on 6-minute walk distance showed that after 52 weeks AT-GAA treated patients (n=20) walked 33 meters farther than their baseline. The alglucosidase alfa treated patients (n=7) walked 38 meters further than their baseline. The difference between the two groups was not statistically significant (p=0.60).

A pre-specified analysis of the patients never previously treated with any ERT showed similar declines in percent-predicted forced vital capacity (FVC) at 52 weeks of –4.1% for AT-GAA treated patients and –3.6% for alglucosidase alpha treated patients. The difference between the two groups was not statistically significant (p=0.57).

6MWD (m) in the ERT Treatment Naive Population

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=20)	393.6 (112.4)	+33.4 (10.9)	-4.9 (19.7)	p=0.60
Alglucosidase alfa (n=7)	420.9 (135.7)	+38.3 (11.1)		

FVC (% predicted) in the ERT Treatment Naive Population

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=20)	80.2 (18.7)	-4.1 (1.5)	-0.5 (2.7)	p=0.57
Alglucosidase alfa (n=7)	79.1 (22.6)	-3.6 (1.8)		

Note: One patient in the alglucosidase alfa arm was excluded from the study analysis due to use of an investigational anabolic like steroid that impacted his baseline performance.

Pre-Specified Analyses of Other Key Secondary and Biomarker Endpoints Across the Overall ERT Switch and ERT Naïve Study Population:

- **Musculoskeletal & Other Key Secondary Endpoints:**
  - **GSGC (Gait, Stairs, Gower's Chair):** GSGC is an important and commonly used endpoint in Pompe Disease capturing strength, coordination and mobility. AT-GAA treated patients demonstrated statistically significant improvements on the scores in this important assessment, compared to a worsening for alglucosidase alfa treated patients in the overall population (p<0.05).
  - **Lower MMT (Manual Muscle Testing), PROMIS Physical Function**: On both of these validated measures of muscle strength and patient reported outcomes, AT-GAA treated patients improved numerically more than alglucosidase alfa treated patients, though the results were not statistically significant.
  - **PROMIS Fatigue:** Fatigue as measured by this scale slightly favored AT-GAA treated patients over alglucosidase alfa treated patients.
- **Biomarkers of Treatment Effects on Disease:**
  - **Urine Hex-4:** For the combined study population of both ERT switch and ERT naïve patients, those patients receiving AT-GAA showed substantial improvements on this biomarker, with a mean reduction of Hex-4 of - 31.5% after 52 weeks compared to an increase of +11.0% (i.e., worsening) in Hex-4 in the alglucosidase alfa treated patients (p=<0.001). Urine Hex-4 is a common biomarker in Pompe disease and is used as an indirect measure of the degree of skeletal glycogen clearance in Pompe patients receiving ERT. Glycogen is the substrate that accumulates in the lysosomes of muscles of Pompe patients.

- **CK (Creatine Kinase):** After 52 weeks, AT-GAA treated patients showed substantial improvements on this biomarker as well with a mean - 22.4% reduction in CK compared to an increase (i.e., worsening) of +15.6% in the alglucosidase alfa treated patients. ($p<0.001$). CK is an enzyme that leaks out of damaged muscle cells and is elevated in Pompe patients.

AT-GAA demonstrated a similar safety profile to alglucosidase alfa. Two patients receiving a AT-GAA (2.4%) discontinued treatment due to an adverse event compared to one (2.6%) for alglucosidase alfa unrelated to treatment. Injection associated reactions (IARs) were reported in 25% of AT-GAA participants and 26% of alglucosidase alfa patients.

John F. Crowley, Chairman and Chief Executive Officer of Amicus Therapeutics, stated, "Based on these data and the entire compelling body of data that we have accumulated over nearly a decade of pre-clinical and clinical studies, we will now advance our plans to obtain regulatory approvals and to bring this medicine to patients worldwide with great urgency. As we have each learned all too well in this past year of COVID, this is a fight now as much against time as it is nature. The global business is now focused across regulatory, manufacturing, medical and all parts of Team Amicus to bring AT-GAA to as many patients as rapidly as possible. We believe that AT-GAA has the potential to quickly become the new standard of care in the treatment of this devastating muscle disease. AT-GAA continues to be the crown jewel of the Amicus portfolio of rare disease medicines and these data represent great hope for a better future for all those living with Pompe disease around the world."

Conference Call and Webcast

Amicus Therapeutics will host a conference call and audio webcast today, February 11, 2021 at 4:30 p.m. ET to discuss the topline PROPEL results. Interested participants and investors may access the conference call by dialing 877-303-5859 (U.S./Canada) or 678-224-7784 (international), conference ID: 3974258.

A live audio webcast and related presentation materials can also be accessed via the Investors section of the Amicus Therapeutics corporate website at ir.amicusrx.com. Web participants are encouraged to register on the website 15 minutes prior to the start of the call. A replay of the call will be available for seven days beginning at 7:30 p.m. ET on February 11, 2021. Access numbers for this replay are 855-859-2056 (U.S./Canada) and 404-537-3406 (international); conference ID: 3974258.

About AT-GAA

AT-GAA is an investigational two-component therapy that consists of cipaglucosidase alfa (ATB200), a unique recombinant human acid alpha-glucosidase (rhGAA) enzyme with optimized carbohydrate structures, particularly bis-phosphorylated mannose-6 phosphate (bis-M6P) glycans, to enhance uptake into cells, administered in conjunction with miglustat (AT2221), a stabilizer of cipaglucosidase alfa. In preclinical studies, AT-GAA was associated with increased levels of the mature lysosomal form of GAA and reduced glycogen levels in muscle, alleviation of the autophagic defect and improvements in muscle strength.

In addition, Amicus is enrolling an open-label, uncontrolled, multicenter study to evaluate the PK, safety, efficacy, and PD of AT-GAA in pediatric patients aged 12 to <18 years with LOPD (ATB200-04). More information, including a list of participating sites, is available at www.clinicaltrials.gov: NCT03911505

About Pompe Disease

Pompe disease is an inherited lysosomal disorder caused by deficiency of the enzyme acid alpha-glucosidase (GAA). Reduced or absent levels of GAA levels lead 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 Statement

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements relating to top-line data from a global Phase 3 study to investigate AT-GAA for the treatment of Pompe Disease 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 Company will not be able to successfully complete the development of, obtain regulatory approval for, or successfully manufacture and 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, 2019 and Quarterly Report on 10-Q for the Quarter ended September 30, 2020. 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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Amicus Therapeutics

AT-GAA (ATB200/AT2221)
Phase 3 PROPEL Topline Results

February 11, 2021

Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements relating to top-line data from a global Phase 3 study to investigate AT-GAA for the treatment of Pompe Disease 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 Company will not be able to successfully complete the development of, obtain regulatory approval for, or successfully manufacture and 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, 2019 and Quarterly Report on 10-Q for the Quarter ended September 30, 2020. 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.

Our Passion for Making a Difference Unites Us

Per Ardua Ad Astra

Amicus Therapeutics

Executive Summary

PROPEL

- Rolling BLA submission for AT-GAA planned for completion in Q2 and other global regulatory submissions for approval expected throughout 2021
- Patients switching to AT-GAA from the approved ERT, alglucosidase alfa, walked +16.9 meters farther than those treated with standard of care ERT (**p=0.046**)
- Patients switching to AT-GAA also showed an improvement in percent-predicted forced vital capacity (FVC), the most important measure of respiratory function in Pompe disease, compared to a decline in patients treated with the currently approved ERT (FVC Diff. + 4.1%; **p=0.006**)
- In the overall study population of ERT experienced and ERT naïve patients, AT-GAA showed a nominally statistically significant and clinically meaningful difference for superiority on the first key secondary endpoint of percent-predicted forced vital capacity compared to patients treated with the currently approved ERT (FVC Diff. + 3.0%; **p=0.023**)
- In the overall study population of ERT experienced and ERT naïve patients, AT-GAA outperformed the currently approved ERT (+21 meters compared to +7 meters) which was not statistically significant for superiority (**p=0.072**)
- Improvements in the two important biomarkers of Pompe disease (Hex-4 and CK) for the overall study population significantly favored AT-GAA compared to the currently approved ERT (**p<0.001**)
- **8 of 8** Key Secondary and Biomarker Endpoints favored AT-GAA compared to standard of care in the overall and ERT experienced population

Amicus Therapeutics

Pompe Disease Overview

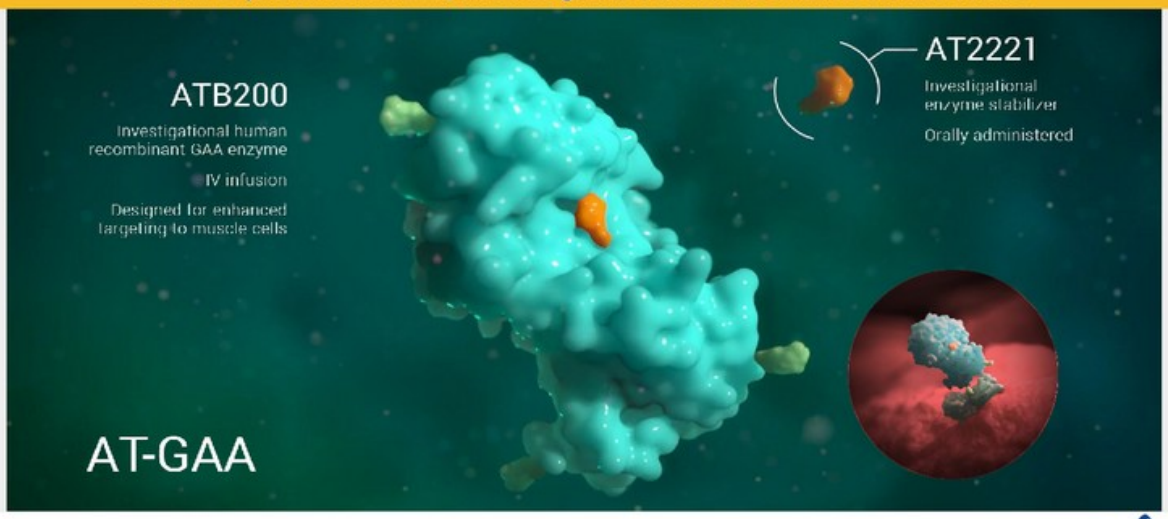
Pompe disease is a severe and fatal neuromuscular disease and one of the most prevalent lysosomal disorders. Despite the majority of diagnosed Pompe patients in the addressable geographies in the world being treated with currently approved ERT alglucosidase alfa, there remains significant unmet medical need

- 5,000 – 10,000+ patients diagnosed WW[1]; newborn screening suggests underdiagnosis
- Age of onset ranges from infancy to adulthood
- Patients on currently approved ERT decline after ~2 years
- Respiratory and cardiac failure are leading causes of morbidity and mortality
- Deficiency of GAA leading to glycogen accumulation and cellular dysfunction
- Symptoms include muscle weakness, respiratory failure, and cardiomyopathy
- $1B+ global Pompe ERT sales[2]

1. National Institute of Neurological Disorders and Stroke (NIH). 2. Based on calendar year ending December 31, 2020. Source: Sanofi Press Releases

AT-GAA: ATB200 (cipaglucosidase alfa) and AT2221 (miglustat)

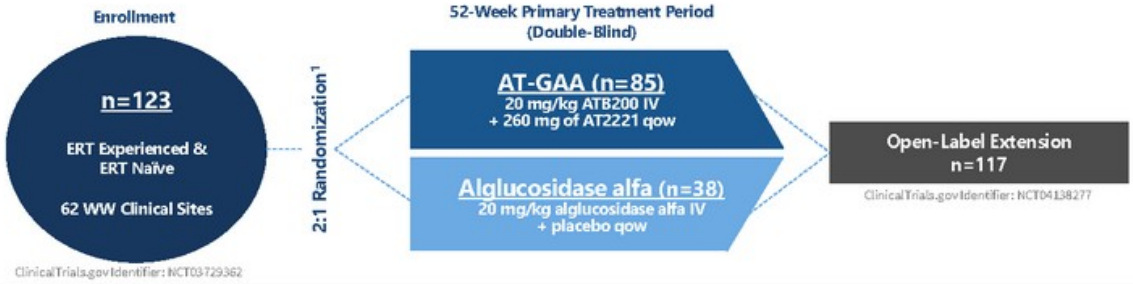
ATB200 is a novel rhGAA being developed as a next-generation enzyme replacement therapy (ERT) for the treatment of Pompe disease, used in conjunction with AT2221, an iminosugar that stabilizes and enhances the PK of ATB200



PROPEL (ATB200-03): Study Design

PROPEL

Phase 3 double-blind randomized study to assess the efficacy and safety of ATB200/AT2221 in adult subjects with late-onset Pompe disease compared with alglucosidase alfa/placebo



Key Enrollment Criteria:

- ≥18 years old, weigh ≥ 40 kg at screening with confirmed diagnosis of LOPD
- Classified as one of the following with respect to ERT status:
  - ERT experienced, defined as currently receiving standard of care ERT (alglucosidase alfa) for ≥24 months
  - ERT naive, defined as never having received ERT
- 6MWD ≥ 75 meters and ≤ 90% of the predicted value for healthy adults at screening
- Sitting FVC ≥ 30% of the predicted value for healthy adults at screening

[1]2:1 randomization with stratification factors on ERT status, baseline 6MWD

Amicus Therapeutics

Study Objectives and Statistical Methods

PROPEL

Primary and Secondary Objectives

To assess the efficacy of AT-GAA compared with alglucosidase alfa/placebo on:

- Ambulatory function, as measured by the 6-minute walk distance (6MWD) [Primary]
- Pulmonary function, as measured by % predicted sitting forced vital capacity (FVC)
- Muscle strength, health related patient reported outcomes (PROs) and motor function

Statistical Methods

- Primary endpoint of 6MWD analyzed using MMRM on ITT observed cases
- All key secondary endpoints including FVC analyzed by ANCOVA with last observation carried forward (ITT LOCF)

Study Endpoints

PROPEL

Primary Endpoint

Change from baseline to Week 52 in 6 Minute Walk Distance (6MWD)

Key Secondary Endpoint

Change from baseline to Week 52 in % predicted sitting Forced Vital Capacity (FVC)

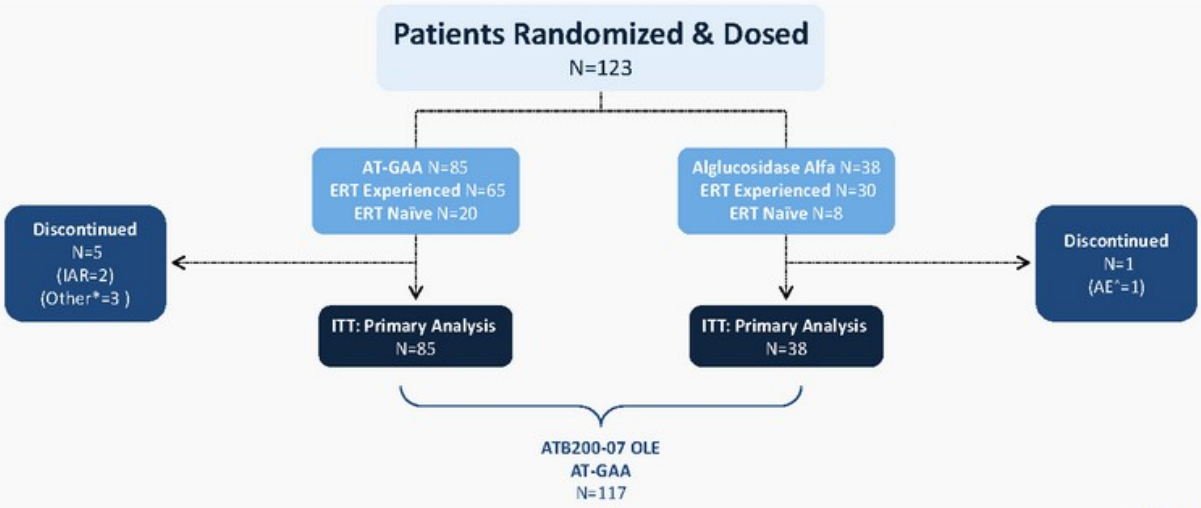
Other Key Secondary Endpoints

- Change from baseline to Week 52 in the manual muscle test (MMT) score for lower extremities
- Change from baseline to Week 52 in the PROMIS® – Physical Function domain score
- Change from baseline to Week 52 in the PROMIS® – Fatigue domain score
- Change from baseline to Week 52 in the GSGC score (Gait, Stairs, Gowers, Chair)

Patient Disposition

PROPEL

There was a very low drop-out rate and all patients completing the study subsequently enrolled in the AT-GAA extension study



Note: * 1 Covid pneumonia, 2 withdrew no longer wanting to travel to sites for infusion all unrelated to study drug; ^1 stroke, unrelated to study drug

Amicus Therapeutics

Baseline Demographics

PROPEL

Baseline demographics were representative of the population and generally similar in the two treatment arms

	AT-GAA n=85	Alglucosidase alfa n=38	Total n=123
Age (years)			
Mean (SD)	47.6 (13.3)	45.1 (13.3)	46.8 (13.3)
Median (Min, Max)	48.0 (19, 74)	46.0 (22, 66)	47.0 (19, 74)
Gender, n (%)			
Male	36 (42.4)	20 (52.6)	56 (45.5)
Female	49 (57.6)	18 (47.4)	67 (54.5)
Previous ERT Duration (ERT Exp. only)			
<3 years	4 (6.2)	5 (16.7)	9 (9.5)
3-5 years	16 (24.6)	6 (20.0)	22 (23.2)
>5 years	45 (69.2)	19 (63.3)	64 (67.4)
Race, n (%)			
White	74 (87.1)	30 (78.9)	104 (84.6)
Asian	5 (5.8)	5 (13.2)	10 (8.1)
Other	6 (7.1)	3 (7.9)	9 (7.3)
Regions, n(%)			
North/South America	26 (30.6)	15 (39.5)	41 (33.3)
Europe	43 (50.6)	12 (31.6)	55 (44.7)
Asia Pacific	16 (18.8)	11 (28.9)	27 (22.0)

Baseline Characteristics

PROPEL

Baseline 6MWD and FVC were representative of the population and generally similar in the two treatment arms

	AT-GAA n=85		Alglucosidase alfa n=37	
6MWD, m				
Mean (SD)	357.9 (111.8)		351 (121.3)	
Median (Min, Max)	359.5 (79.0, 575.0)		365.5 (112.5, 623.0)	
	ERT Experienced	**ERT Naive**	**ERT Experienced**	**ERT Naive**
	n=65	n=20	n=30	n=7
Mean (SD)	346.9 (110.2)	393.6 (112.4)	334.6 (114.0)	420.9 (135.7)
Median (Min, Max)	352.5 (79.0, 557.5)	375.2 (154.0, 575.0)	343.5 (112.5, 532.3)	385.5 (201.0, 623.0)

	AT-GAA n=85		Alglucosidase alfa n=37	
FVC % Predicted, Sitting				
Mean (SD)	70.7 (19.6)		69.7 (21.5)	
Median (Min, Max)	70.0 (30.5, 132.5)		71.0 (31.5, 122.0)	
	ERT Experienced	**ERT Naive**	**ERT Experienced**	**ERT Naive**
	n=65	n=20	n=30	n=7
Mean (SD)	67.9 (19.1)	80.2 (18.7)	67.5 (21.0)	79.1 (22.6)
Median (Min, Max)	68 (30.5, 132.5)	82.3 (48.0, 111.0)	69.0 (31.5,122.0)	93.5 (46.5, 98.0)

6MWD=6-minute walk distance; FVC=forced vital capacity

Results exclude one clinically implausible patient who used an investigational anabolic steroid ostarine (selective androgen receptor modulator) just prior to study start.

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6MWD and FVC Results: Overall Population (n=122)

PROPEL

6MWD showed greater improvement with AT-GAA versus alglucosidase alfa but did not demonstrate statistical superiority; FVC demonstrated clinically significant improvement with AT-GAA over alglucosidase alfa

6MWD (m)

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=85)	357.9 (111.8)	+20.8 (4.6)	+13.6 (8.3)	p=0.072
Alglucosidase alfa (n=37)	351.0 (121.3)	+7.2 (6.6)		

FVC (% predicted)

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=85)	70.7 (19.6)	-0.9 (0.7)	+3.0 (1.2)	**p=0.023**
Alglucosidase alfa (n=37)	69.7 (21.5)	-4.0 (0.8)		

NOTES: Baseline is Mean (STDEV); CFBL is Mean LOCF (SE); P-values are nominal 2-sided; FVC data normally distributed and p–values are from ANCOVA.
Results exclude one clinically implausible patient who used an investigational anabolic steroid ostarine (selective androgen receptor modulator) just prior to study start.
6MWD data not normally distributed and 6MWD p-value is for non-parametric ANCOVA; 6MWD parametric MMRM p-value was p=0.097.

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6MWD and FVC Results: ERT Experienced Population (n=95)

PROPEL

In the ERT experienced population there was a clinically significant improvement in both 6MWD and FVC with AT-GAA over alglucosidase alfa

6MWD (m)

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=65)	346.9 (110.2)	+16.9 (5.0)	+16.9 (8.8)	p=0.046
Alglucosidase alfa (n=30)	334.6 (114.0)	0.0 (7.2)		

FVC (% predicted)

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=65)	67.9 (19.1)	+0.1 (0.7)	+4.1 (1.2)	p=0.006
Alglucosidase alfa (n=30)	67.5 (21.0)	-4.0 (0.9)		

NOTE: Baseline is Mean (STDEV); CFBL is Mean LOCF (SE); P-values are nominal 2-sided; FVC data normally distributed and p-values are from ANCOVA
6MWD data not normally distributed and 6MWD p-value is for non-parametric ANCOVA; 6MWD parametric MMRM p-value was p=0.078

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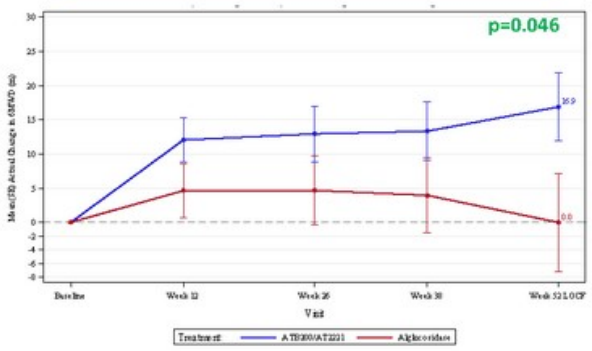
6MWD and FVC Plots: ERT Experienced Population (n=95)

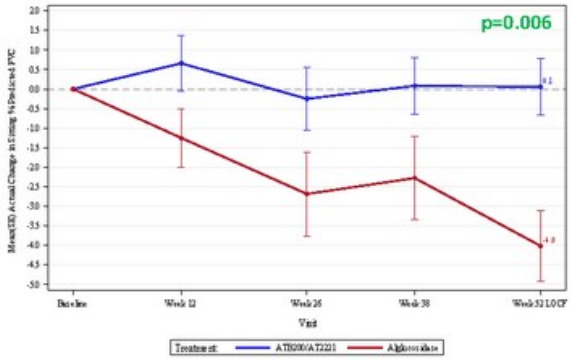
PROPEL

ERT experienced patients treated with AT-GAA demonstrated improvements over time in 6MWD and stabilization over time in FVC versus alglucosidase alfa

6MWD (m): Change from baseline (n=65, n=30)



FVC (% predicted): Change from baseline (n=65, n=30)



NOTE: Baseline is Mean (STDEV); CFBL is Mean (SE); P-values are nominal 2-sided; FVC data normally distributed and p-values are from ANCOVA
6MWD data not normally distributed and 6MWD p-value is for non-parametric ANCOVA; 6MWD parametric MMRM p-value was p=0.078

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6MWD and FVC Results: ERT Naive Population (n=27)

PROPEL

In the smaller ERT naive population, variability was greater and 6MWD and FVC both numerically favored alglucosidase alfa

6MWD (m)

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=20)	393.6 (112.4)	+33.4 (10.9)	-4.9 (19.7)	p=0.60
Alglucosidase alfa (n=7)	420.9 (135.7)	+38.3 (11.1)		

FVC (% predicted)

Treatment	Baseline	CFBL at Week 52	Difference	P-Value
AT-GAA (n=20)	80.2 (18.7)	-4.1 (1.5)	-0.5 (2.7)	p=0.57
Alglucosidase alfa (n=7)	79.1 (22.6)	-3.6 (1.8)		

NOTES: Baseline is Mean (STDEV); CFBL is Mean LOCF (SE); P-values are nominal 2-sided; FVC data normally distributed and p-values are from ANCOVA.
Results exclude one clinically implausible patient who used an investigational anabolic steroid ostarine (selective androgen receptor modulator) just prior to study start.
6MWD data not normally distributed and p-value is for Wilcoxon Test; 6MWD parametric MMRM p-value was p=0.75

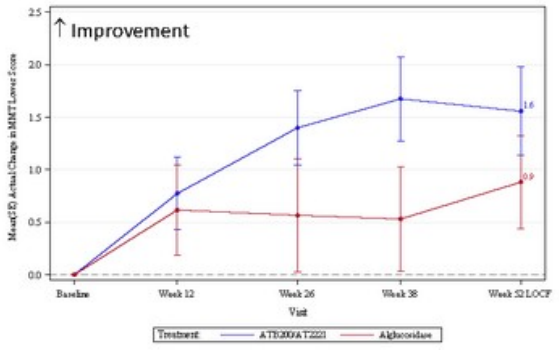
Key Secondary: Lower MMT

All Patients & ERT Experienced Patients

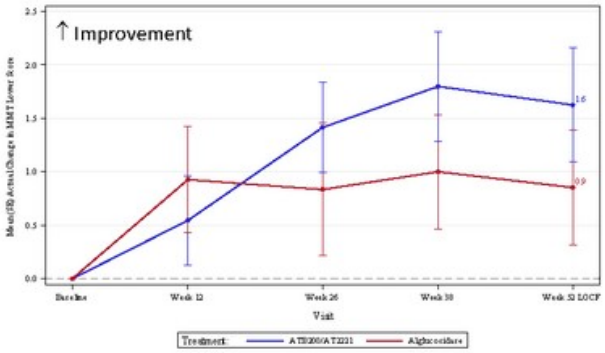
PROPEL

In the overall population and ERT experienced population lower MMT numerically favored AT-GAA

Overall Population



ERT Experienced Population



Note: MMT measured via the Medical Research Criteria (MRC) scale

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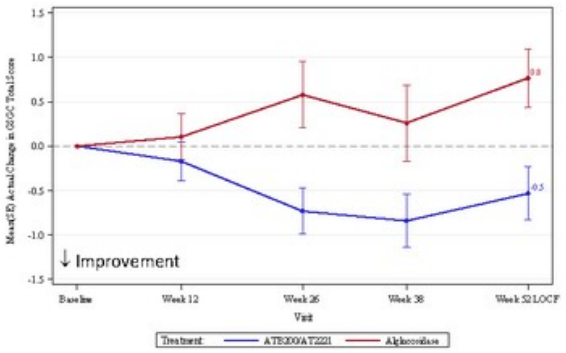
Key Secondary: GSGC (Gait, Stairs, Gowers, Chair)

All Patients & ERT Experienced Patients

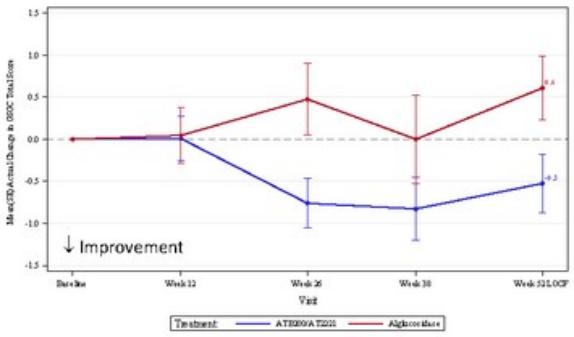
PROPEL

In the overall population and ERT experienced population clinically significant improvement was observed in GSGC with AT-GAA

Overall Population



ERT Experienced Population



Note: GSGC total score is the sum of 4 tests and ranges from a minimum of 4 points (normal performance) to a maximum of 27 points (worst score).

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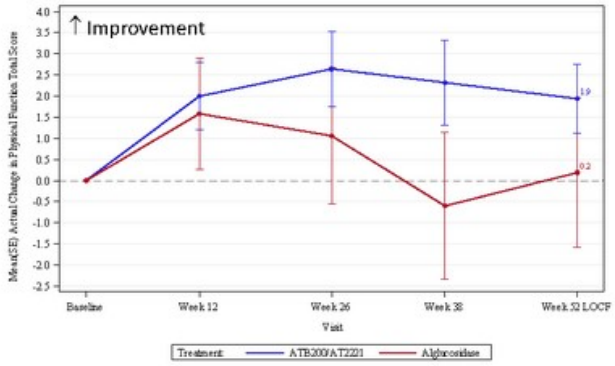
Key Secondary: PROMIS Physical Function

All Patients & ERT Experienced Patients

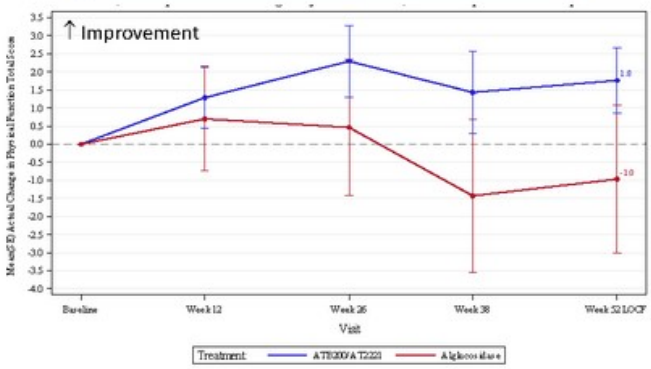
PROPEL

In the overall population and ERT experienced population PROMIS physical function numerically favored AT-GAA

Overall Population



ERT Experienced Population



Note: PROMIS – Physical Function Short Form 20a (v2.0) consists of 20 questions scored on a scale from 1 to 5: 1 = unable to do; 5 = not at all; min score 20 max score 100

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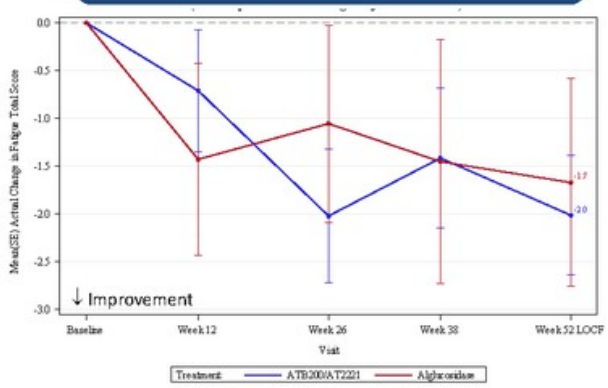
Key Secondary: PROMIS Fatigue

All Patients & ERT Experienced Patients

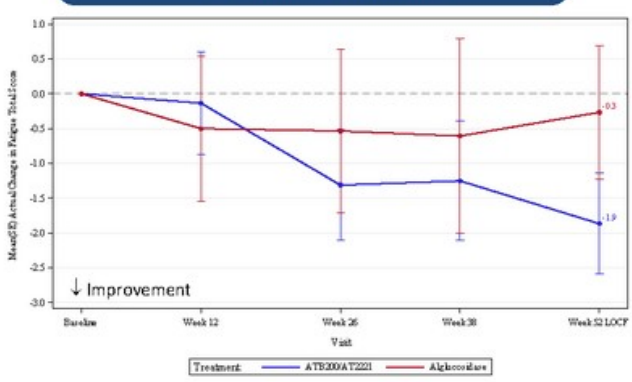
PROPEL

In the overall population and ERT experienced population PROMIS fatigue numerically favored AT-GAA

Overall Population



ERT Experienced Population



Note: PROMIS – Fatigue Short Form 8a consists of 8 questions scored on a scale from 1 to 5: 1 = not at all; 5 = very much min score 8 max score 40

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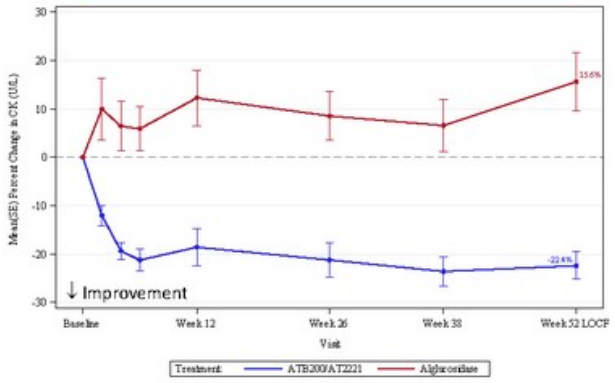
Biomarker: Creatine Kinase (CK)

All Patients & ERT Experienced Patients

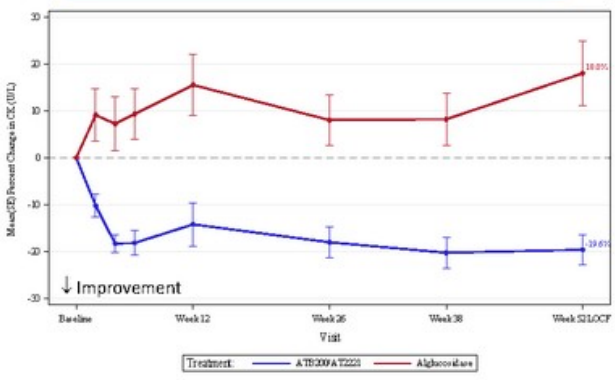
PROPEL

In the overall population and ERT experienced population reductions in CK were significantly greater with AT-GAA

Overall Population



ERT Experienced Population



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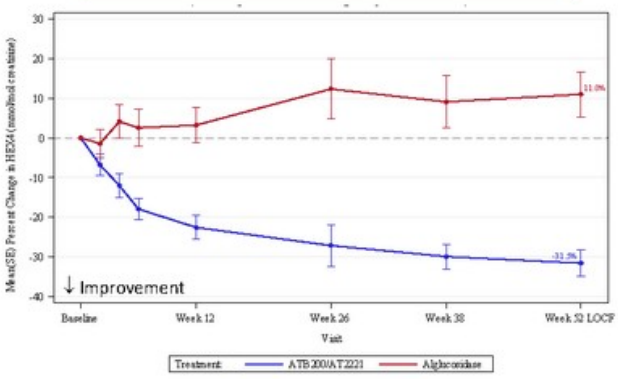
Biomarker: Urinary Hex4

All Patients & ERT Experienced Patients

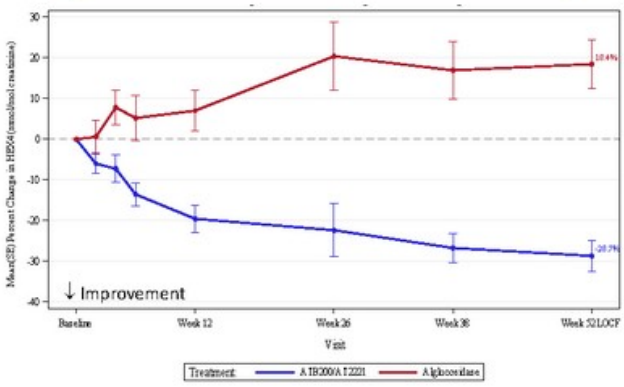
PROPEL

In the overall population and ERT experienced population reductions in Hex4 were significantly greater with AT-GAA

Overall Population



ERT Experienced Population



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Primary, Key Secondary and Biomarker Endpoint Heat Map

All Patients & ERT Experienced Patients

Endpoints across motor function, pulmonary function, muscle strength, PROs and biomarkers favored AT-GAA over alglucosidase alfa in both the overall and ERT experienced populations

Overall Population

	Alglucosidase alfa	AT-GAA
Motor Function		6MWD
		GSGC*
Pulmonary Function		FVC*
Muscle Strength		Lower MMT
PROs		PROMIS-Physical
		PROMIS-Fatigue
Biomarker		Hex4*
		CK*

ERT Experienced Population

	Alglucosidase alfa	AT-GAA
Motor Function		6MWD*
		GSGC*
Pulmonary Function		FVC*
Muscle Strength		Lower MMT
PROs		PROMIS-Physical
		PROMIS-Fatigue
Biomarker		Hex4*
		CK*

Note: * Nominal P-value <0.05; based on LOCF means

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Safety Summary

PROPEL

Safety profile was similar for AT-GAA and alglucosidase alfa

	AT-GAA n=85	Alglucosidase Alfa n=38
TEAEs	81 (95.3%)	37 (97.4%)
TEAEs Potentially Related to Treatment	26 (30.6%)	14 (36.8%)
Serious TEAEs	8 (9.4%)	1 (2.6%)
Serious TEAEs Potentially Related to Treatment	1 (1.2%)	0
TEAEs Leading to Study Withdrawal	2 (2.4%)	1 (2.6%)
TEAEs Leading to Death	0	0
IARs	21 (24.7%)	10 (26.3%)

- TEAEs leading to withdrawal in the AT-GAA arm were two IARs, one of which was a serious AE
- TEAEs leading to withdrawal in the alglucosidase arm was due to stroke (unrelated)
- Overall safety profile of AT-GAA is similar to alglucosidase alfa

AT-GAA: Next Steps

PROPEL

- Rolling BLA submission expected to complete in Q2
- Other key regulatory submissions for approval throughout 2021 including MAA in Europe
- Potential for early approval under EAMS framework with Priority Innovative Medicines Designation in UK
- 150+ patients worldwide now being treated with AT-GAA including adults, adolescents and infants
- Pediatric study for Pompe patients aged 12 to <18 with late-onset Pompe disease ongoing
- Clinical study for Pompe patients with infantile onset disease expected to begin this year
- Expanded access program for Pompe infantile patients and adult-onset patients open and has enrolled multiple patients with Pompe. Further expanded access for all Pompe patients being considered.

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PROPEL

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Thank You
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