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







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

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

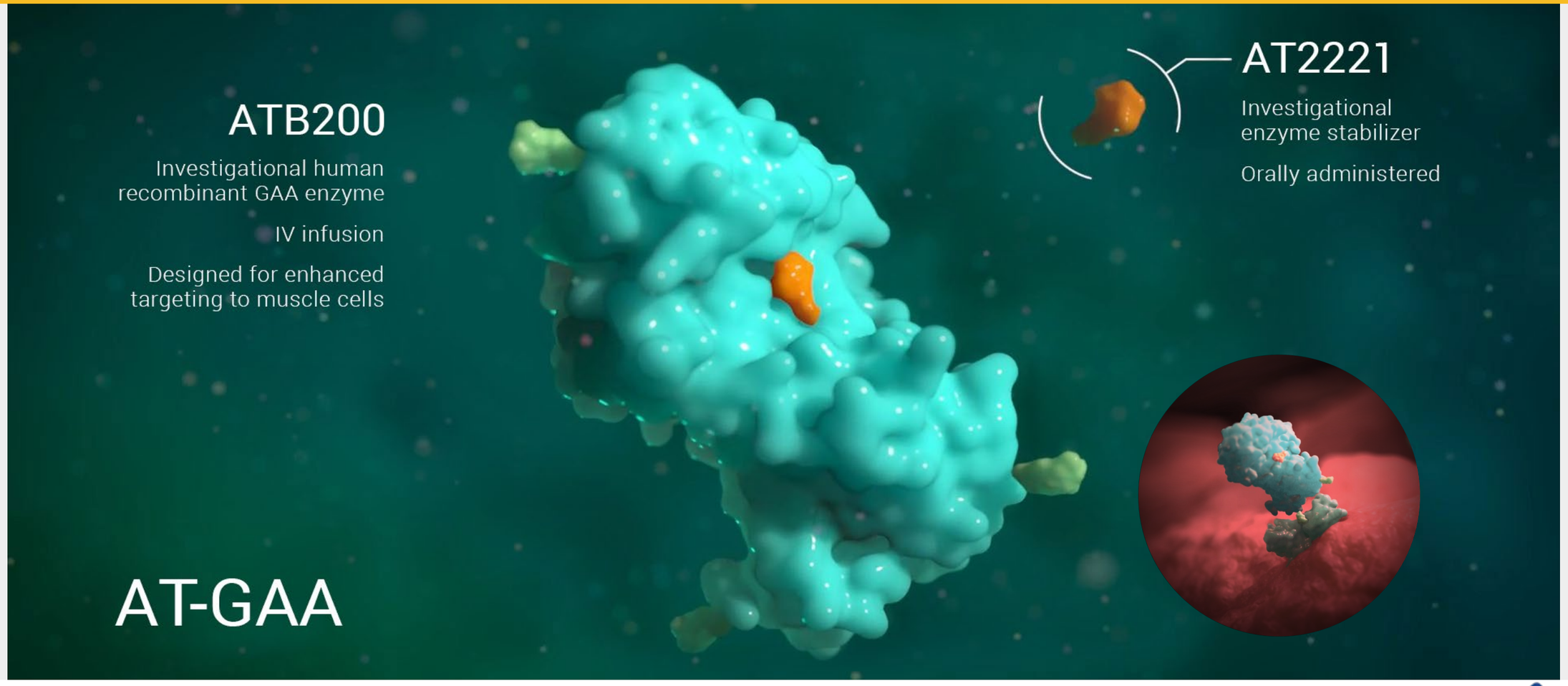
Symptoms include muscle weakness, respiratory failure, and cardiomyopathy

$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

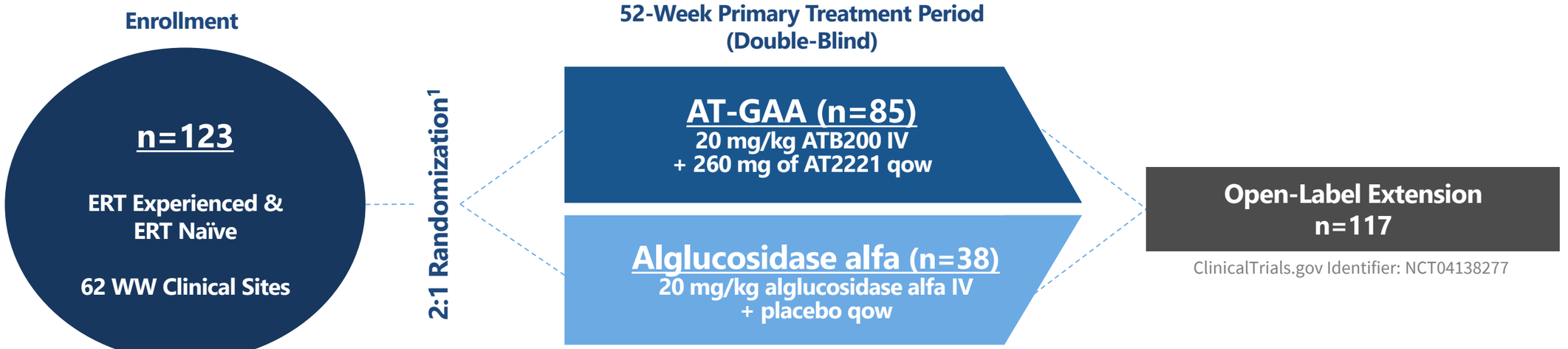
AT-GAA: ATB200 (cipaglucosidase alfa) and AT2221 (miglustat)

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

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 naïve, 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

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)

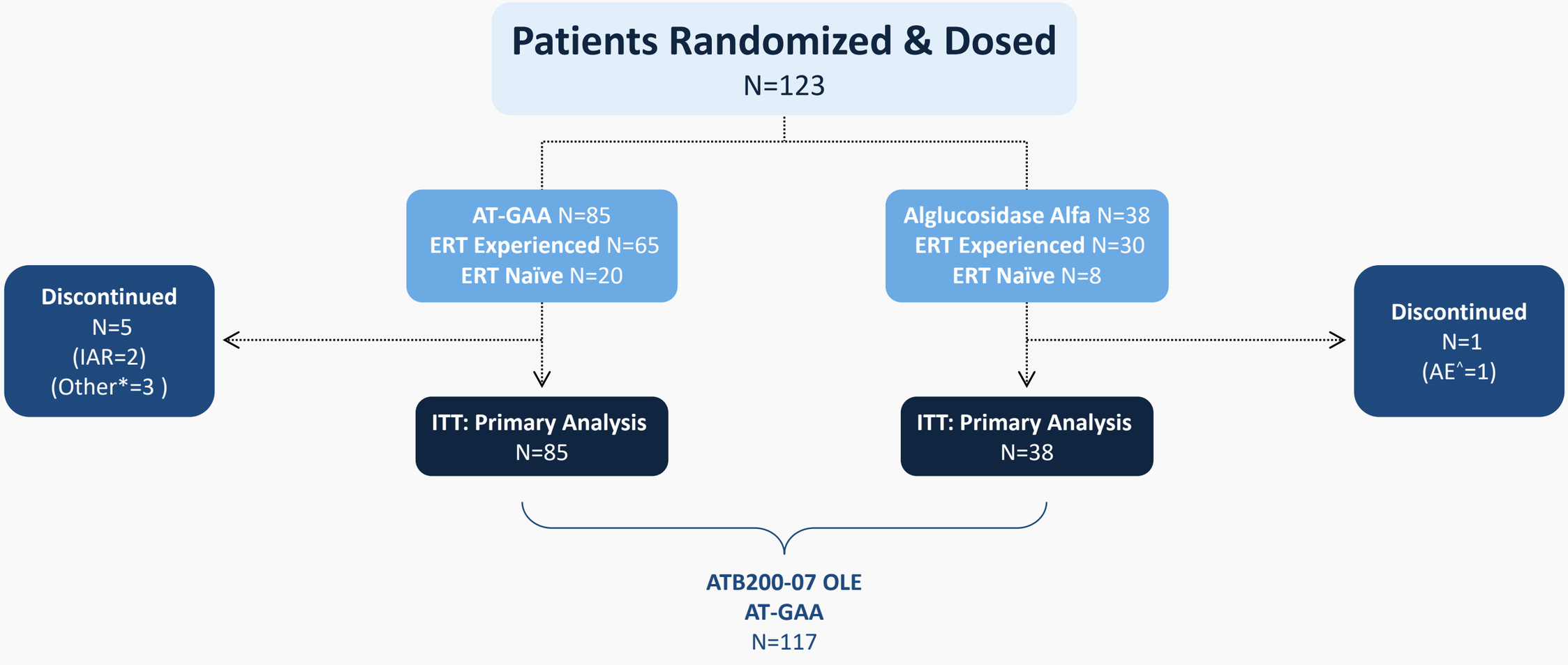
Other Key Secondary Endpoints

- 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.

Amicus Therapeutics

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.

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)		

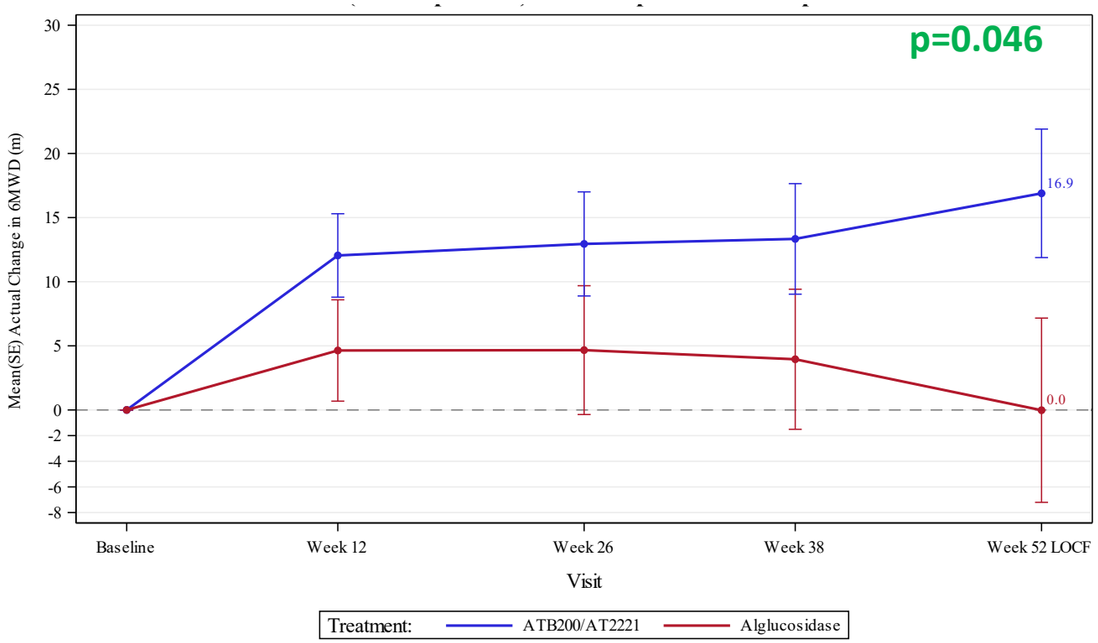
NOTE: Baseline is Mean (STDEV); CFBL is Mean LOCF (SE); P-values are nominal 2-sided; FVC data normally distributed and p–values are from ANCOVA
6MWD data not normally distributed and 6MWD p-value is for non-parametric ANCOVA; 6MWD parametric MMRM p-value was p=0.078

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

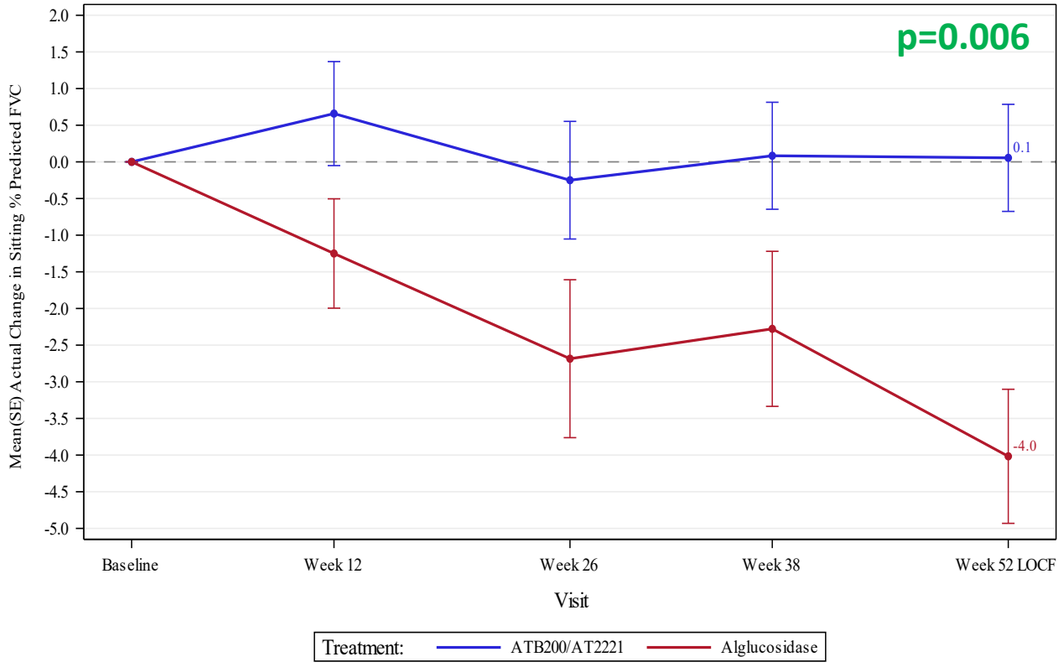
PROPEL

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

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

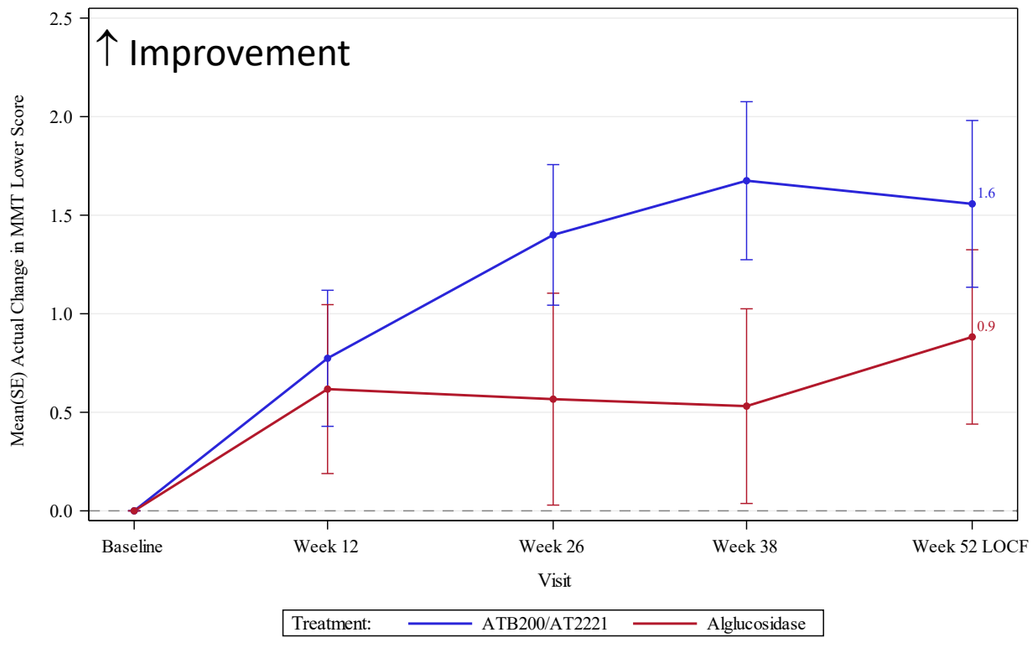
Key Secondary: Lower MMT

All Patients & ERT Experienced Patients

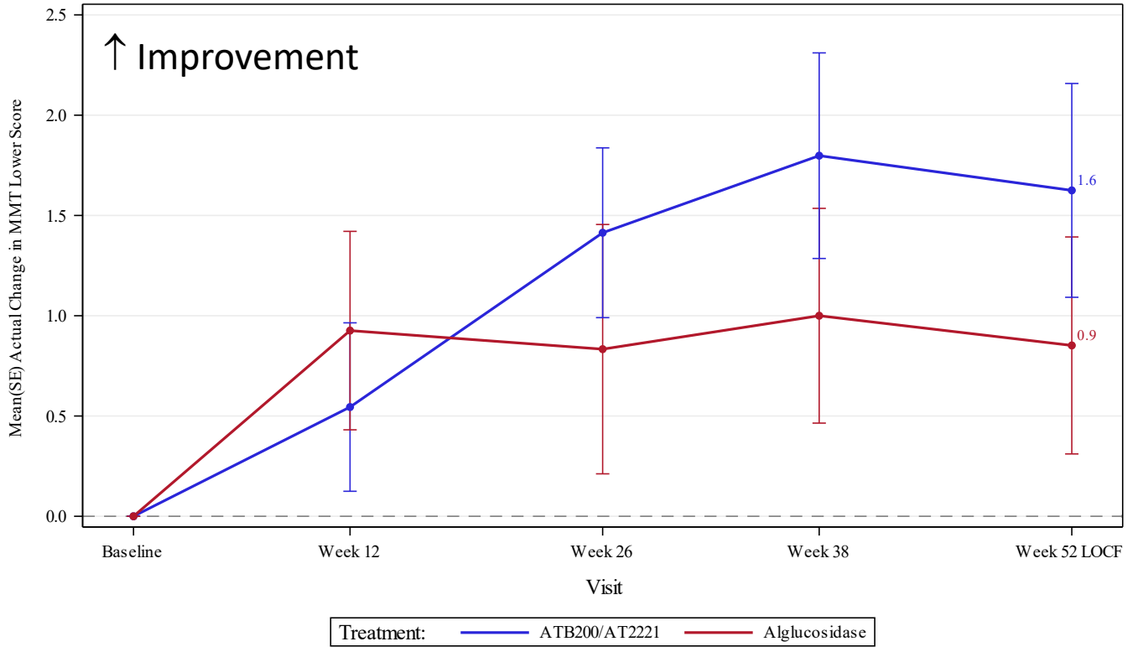
PROPEL

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

Overall Population



ERT Experienced Population



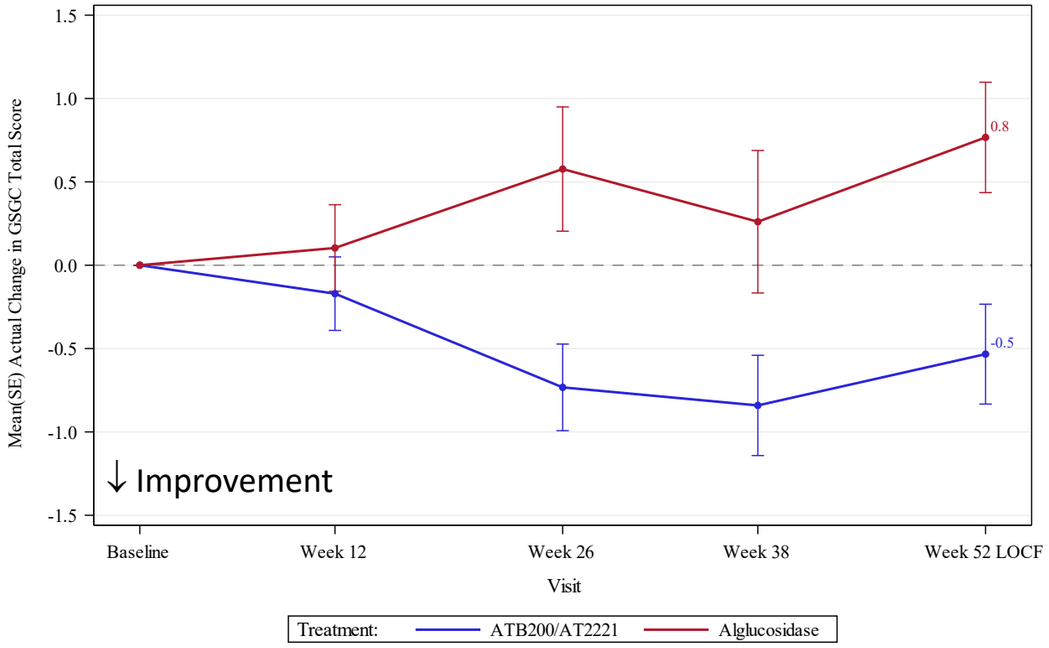
Note: MMT measured via the Medical Research Criteria (MRC) scale

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

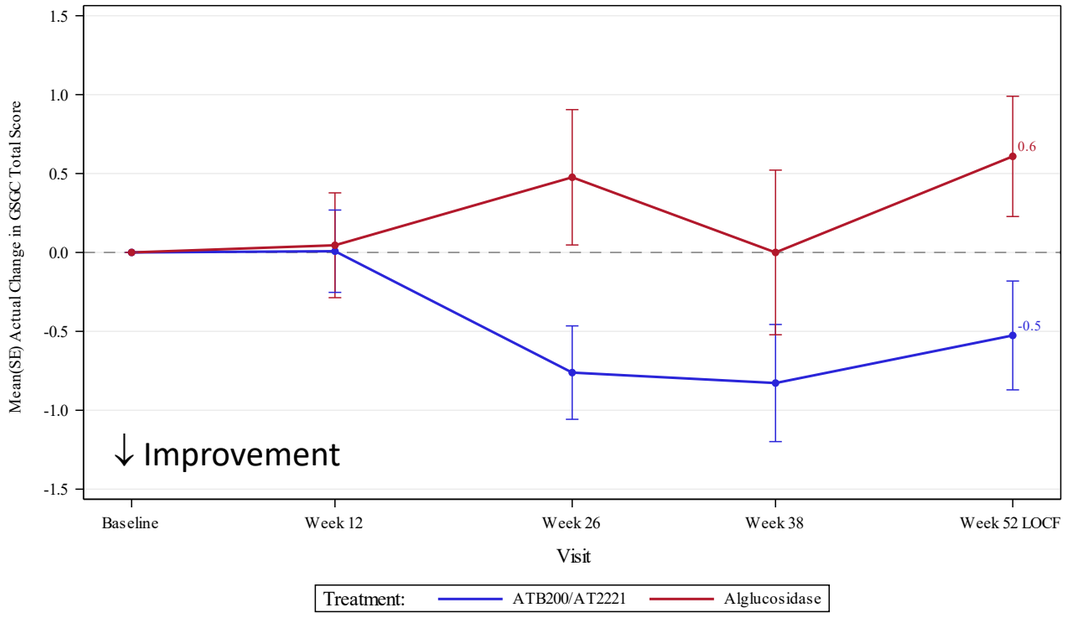
All Patients & ERT Experienced Patients

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).

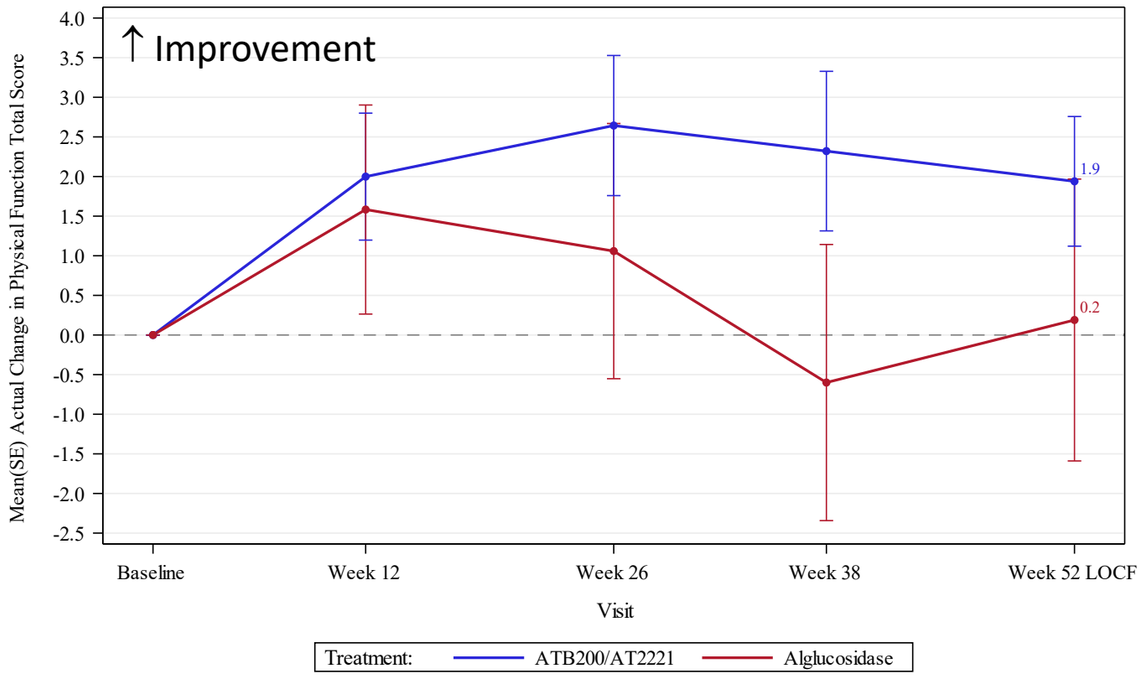
Key Secondary: PROMIS Physical Function

All Patients & ERT Experienced Patients

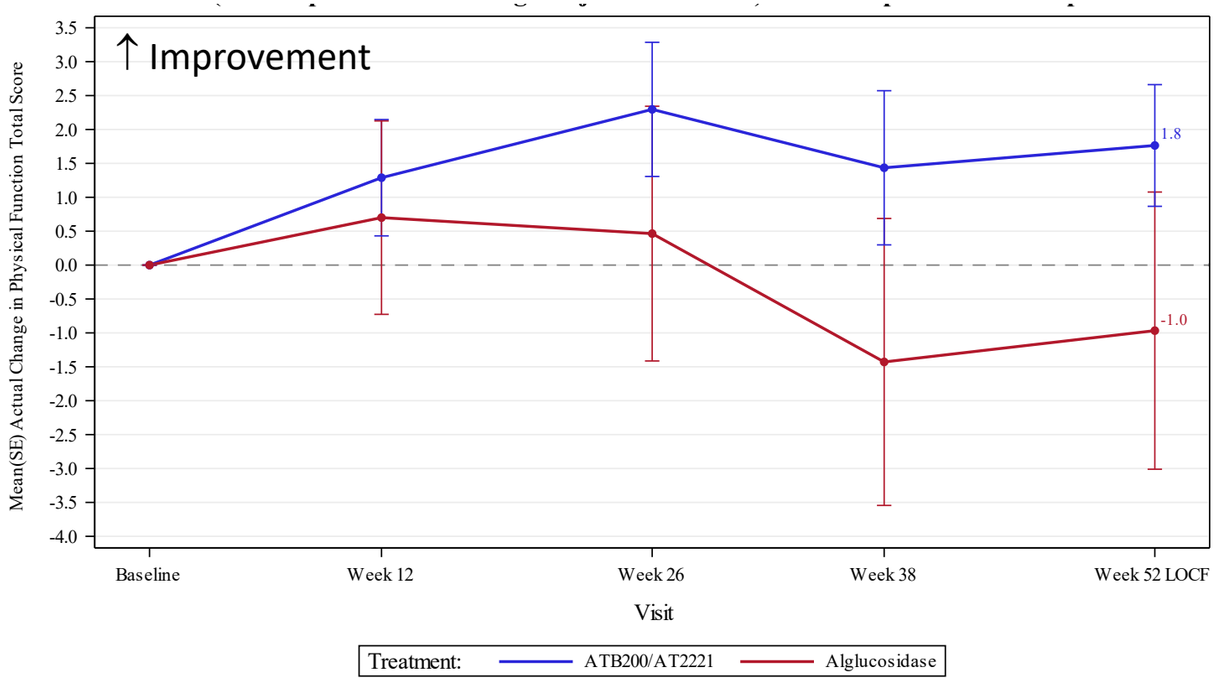
PROPEL

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

Overall Population



ERT Experienced Population



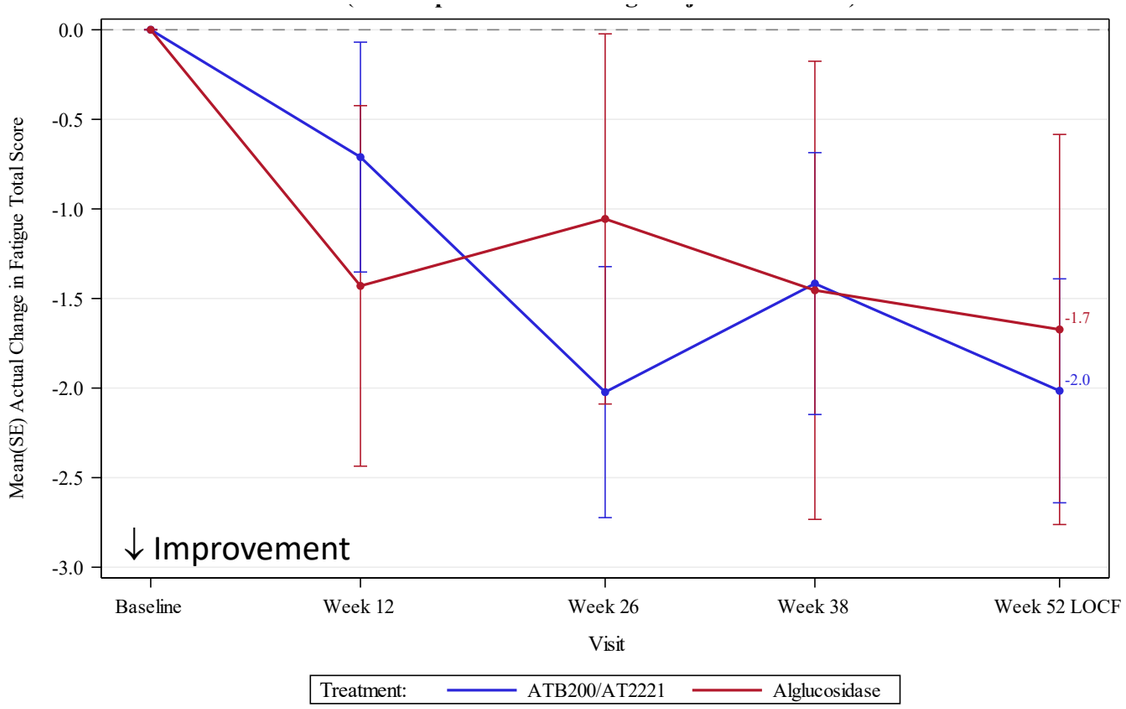
Note: PROMIS – Physical Function Short Form 20a (v2.0) consists of 20 questions scored on a scale from 1 to 5: 1 = unable to do; 5 = not at all; min score 20 max score 100

Key Secondary: PROMIS Fatigue

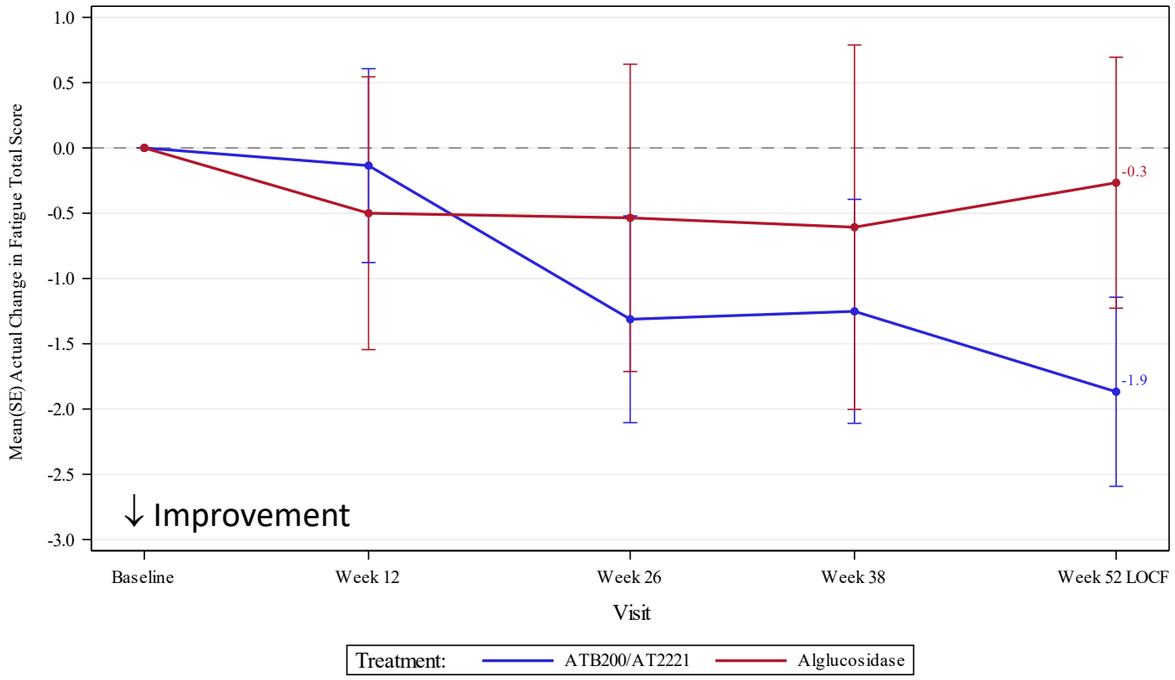
All Patients & ERT Experienced Patients

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

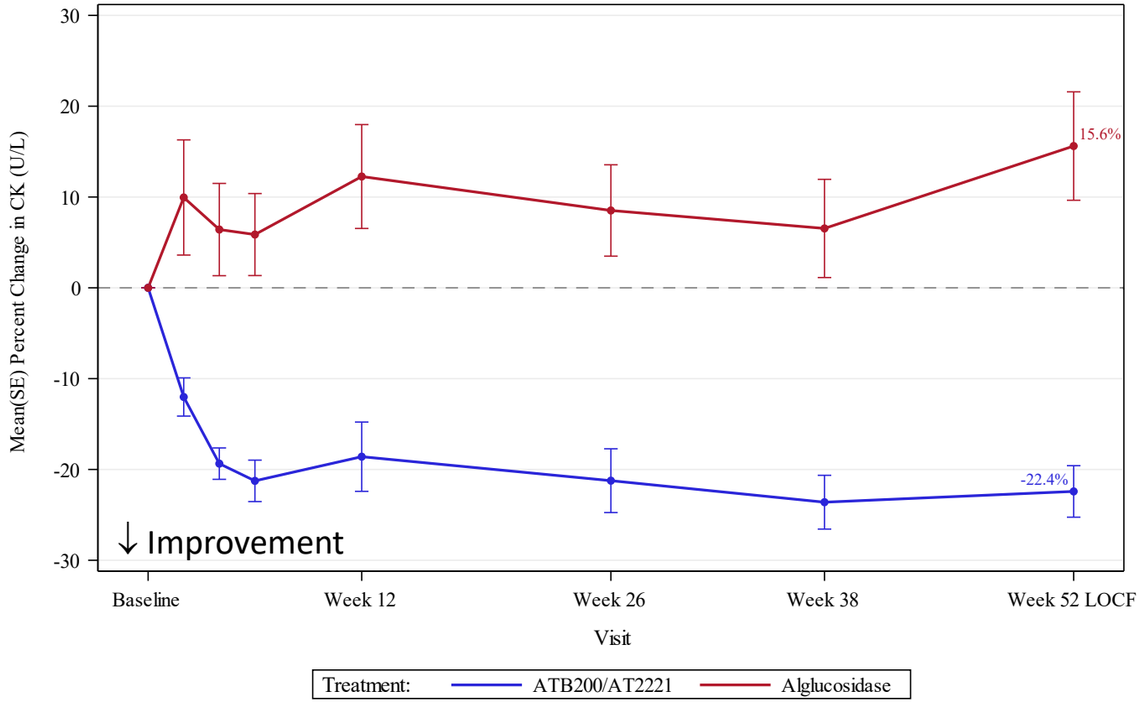
Biomarker: Creatine Kinase (CK)

All Patients & ERT Experienced Patients

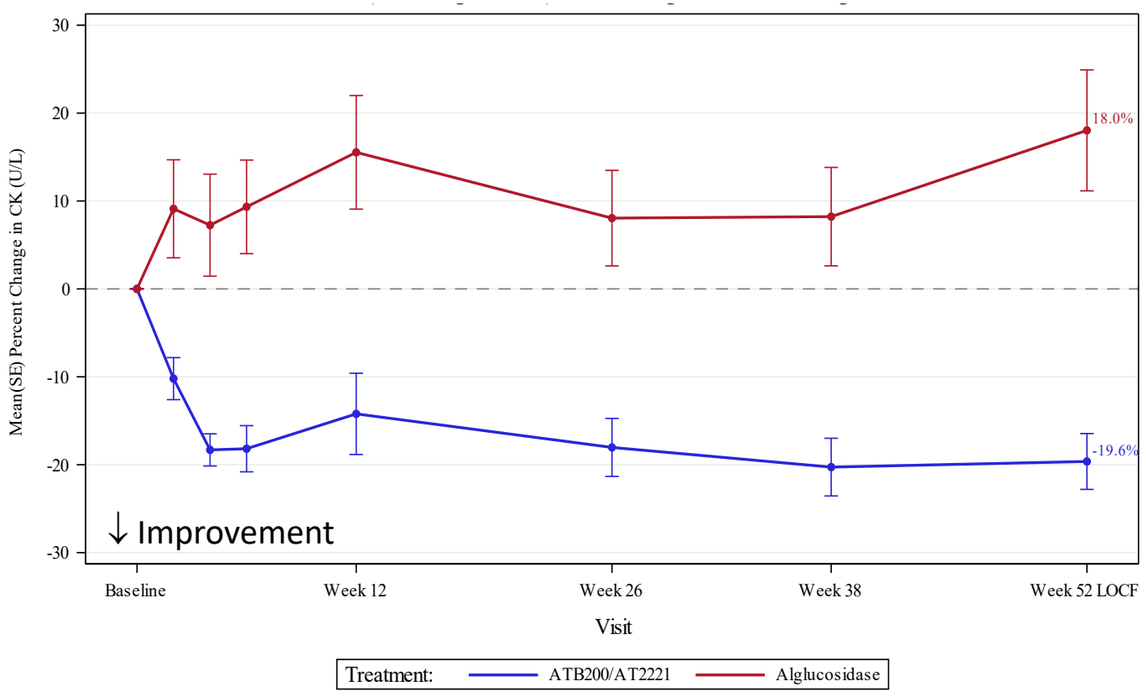
PROPEL

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

Overall Population



ERT Experienced Population



Amicus Therapeutics

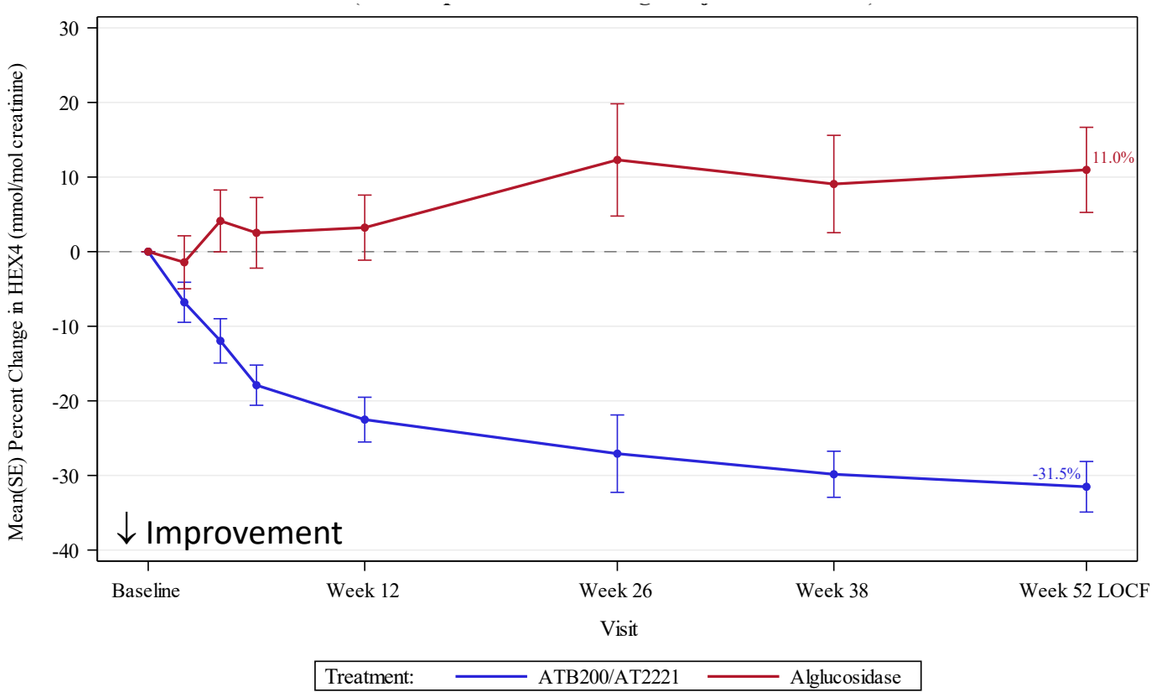
Biomarker: Urinary Hex4

All Patients & ERT Experienced Patients

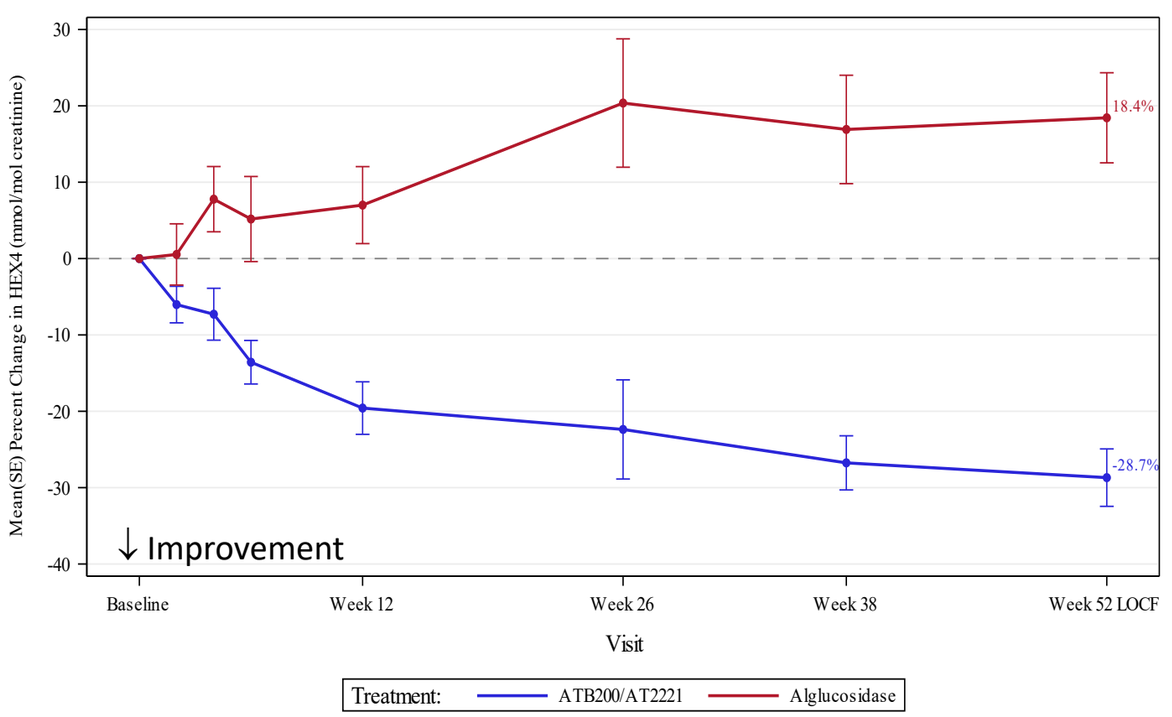
PROPEL

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

Overall Population



ERT Experienced Population



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

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

AT-GAA for Pompe Advances Toward Approval

- 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.

Acknowledgments

- Amicus thank the patients, their families, and Pompe disease patient organizations for their participation in the PROPEL study sponsored by Amicus Therapeutics
- Amicus would also like to thank the investigators, and site staff for their support and contributions in the PROPEL study

Hashiguchi Akihiro MD	Ozlem Goker-Alpan MD	Giancarlo Parenti MD
Hernan Amartino MD	Robert Henderson MD	Helio Pedro MD
Prof. Henning Andersen MD	Shinichi Hirose MD	Alan Pestronk MD
Stephen Arbogast MD	Tarekegn Hiwot MD	Colin Quinn MD
Shahram Attarian MD	Robert Hopkin MD	Mark Roberts MD
Halina Bartosik-Psujek MD	Derralynn Hughes MD	Tobias Ruck MD
Martin Bialer MD PhD	Jozsef Janszky MD	Richard Roxburgh MD
Cynthia Bodkin MD	Aneal Khan MD	Sabrina Sacconi MD
Francoise Bouhour MD	Priya Kishnani MD	Tomo Sawada MD
Drago Bratkovic MD	Hiroshi Kobayashi MD	Prof. Benedikt Schoser MD
Thomas Burrow MD	Blaž Koritnik MD	Jin-Hong Shin MD
Ernest Butler, MD	Kornblum Cornelia MD	Hideaki Shiraishi MD
Barry Byrne, MD, PhD	Hani Kushlaf MD	Celine Tard MD
Yin-Hsiu Chien MD	Prof. Laforet Pascal MD, PhD	Ivaylo Tarnev MD
Prof. Kristl Claeys MD PhD	Heather Lau MD	Mark Tarnopolsky MD
Paula R. Clemens MD	Prof. Christopher Lindberg MD	Michel Tchan MD
Patrick Deegan MD	Nicola Longo MD	Prof. Antonio Toscano MD
Jordi Diaz Manera MD	Wolfgang Löscher MD	Prof. Ans van der Ploeg MD
Mazen Dimachkie MD	Prof. Maria Judit Molnar MD	Jaime Vengoechea MD
Aleksandra Dominovic-Kovacevic MD	Tahseen Mozaffar MD	Vescei Laszlo MD
Miriam Freimer MD	George Konstantinos Papadimas MD	

Thank You

Amicus Therapeutics®