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 12, 2020**

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 February 12, 2020, Amicus Therapeutics, Inc. released presentation materials it plans to use in meetings with investors and analysts. A copy of this presentation is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits:

Exhibit No.	Description
99.1	February 12, 2020 Presentation

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.

AMICUS THERAPEUTICS, INC.

Date: February 12, 2020

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

Amicus Therapeutics®

Perspectives on Pompe:

Progress, Persistence and Passion

February 12, 2020

Forward-Looking Statements

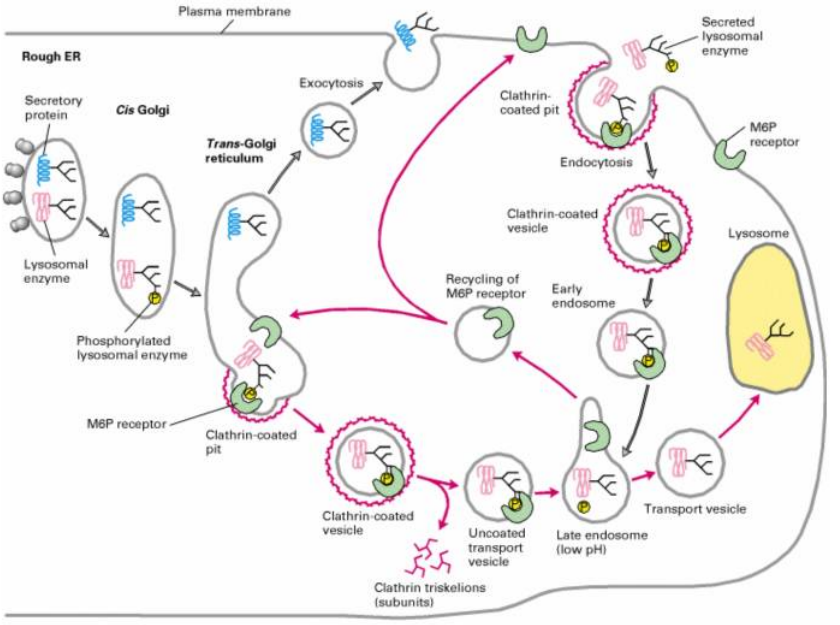
This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 rela scientific theories regarding our product candidate and to preclinical and clinical development of our product candidates. The inclu forward-looking statements should not be regarded as a representation by us that any of our plans will be achieved. Any or all forward-looking statements in this presentation may turn out to be wrong and can be affected by inaccurate assumptions we might m by known or unknown risks and uncertainties. For example, with respect to statements regarding scientific theories about our p candidate and those of our competitors, those theories may prove incorrect and inconsistent with known, unknown or future da statements regarding the results of our preclinical studies and clinical trials, actual results may differ materially from those set forth release due to the risks and uncertainties inherent in our business, including, without limitation: the potential that anecdotal or cas information may materially differ from the actual results of clinical or preclinical studies; the potential that results of clinical or pre studies indicate that the product candidates are unsafe or ineffective in the studied populations or in populations not included in the the potential that regulatory authorities, including the FDA, EMA, and PMDA, may not grant or may delay approval for our p candidates; the potential that preclinical and clinical studies could be delayed because we identify serious side effects or other safety the potential that we may not be able to manufacture or supply sufficient clinical or commercial products; and the potential that we w additional funding to complete all of our studies and manufacturing. Further, the results of earlier preclinical studies and/or clinical tria not be predictive of future results. In addition, all forward-looking statements are subject to other risks detailed in our Annual Report o 10-K for the year ended December 31, 2018. You are cautioned not to place undue reliance on these forward-looking statements, speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, and we und no obligation to revise or update this news release to reflect events or circumstances after the date hereof.

Importance of Properly Glycosylated rhGAA for Treating Pompe Disease

Hung Do, Ph.D., Chief Science Officer

"We encourage and embrace constant innovation
- Amicus Belief Statemer

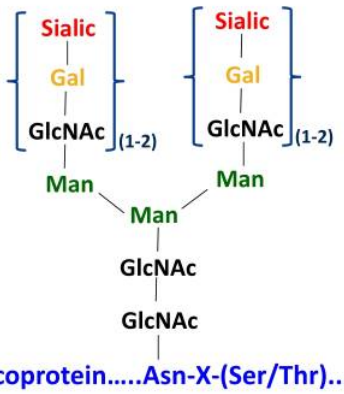
Carbohydrates Are Critical for Sorting and Transporting Proteins From Wi and Outside of Cells



Lodish H, Berk A, Zipursky SL, et al. Molecular Cell Biology. 4th edition. New York: W. H. Freeman; 2000. Section 17.7

- ***ALL*** lysosomal, ER, Golgi, secretory (e.g., antibodies and clotting factors), membrane, a peroxisomal and most mitochondrial protein synthesized in ER
- Processing of N-linked carbohydrates on glycoproteins in Golgi provide specific inform for sorting proteins (analogous to zip codes fo sorting mail)
- Intracellular membrane-bound compartment called vesicles, package and transport protei different organelles, to cell surface or out of c
- Specific carbohydrate receptors on cell surfac enable uptake of exogenous proteins contain appropriate carbohydrates → basis for ERT a GTx

N-Linked Carbohydrate Processing is Complicated and Extremely Difficult Regulate in Production Cells



Key:

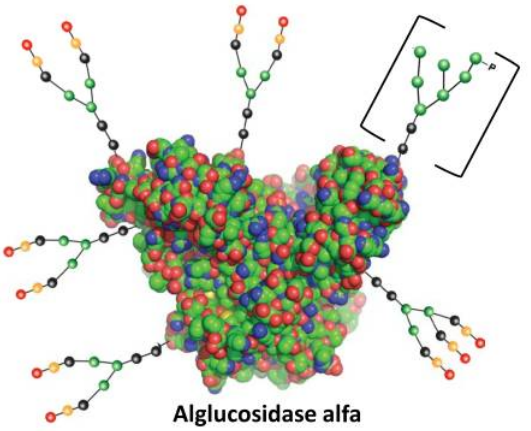
Glc = glucose	Gal = galactose
Man = mannose	GlcNAc = N-acetylglucosamine
GlcNAc = N-acetylglucosamine	Sial = Sialic acid

- Vast majority of proteins synthesized in ER are modified with asparagi (N)-linked carbohydrates (N-glycans) during protein translation
  - Identical N-glycan structure (Glc3-Man9-GlcNAc2) added to all proteins
  - N-glycans helps to define protein domains during initial stages of protein fold and for mediating ER quality control for newly synthesized proteins

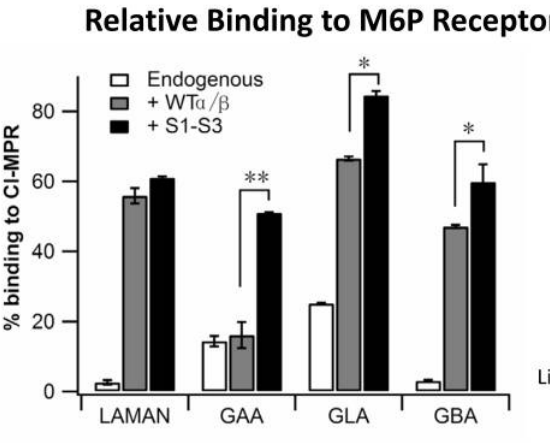
  Glc-Man9 N-glycan structure is binding motif for Calnexin- ER QC (ens only properly folded proteins can leave ER)

  Protein sorting (analogous to assigning zip codes) for protein transpor other cellular and extracellular destinations is mediated by N-glycan processing
- The majority of the N-glycan processing occurs in the Golgi apparatus
  - ***Phosphotransferase*** modifies certain terminal mannose residues to form ma 6-Phosphate (M6P) for lysosomal targeting; prevents further mannose trimn
  - Non-phosphorylated N-glycans are trimmed down to Man5 and no longer al be phosphorylated
  - Non-phosphorylated N-glycans are processed to complex-type N-glycans (ty serum proteins like clotting factors, antibodies, etc.

GAA Is Inherently Poorly Phosphorylated in Cells



Alglucosidase alfa

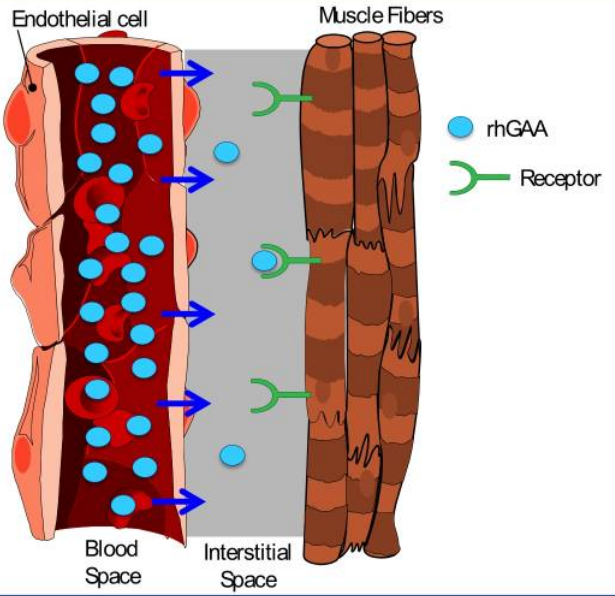


Liu et al., 2

- rhGAA is among a group of lysosomal enzymes that are inherently poorly phosphorylated
  - Phosphotransferase is limiting in cells
  - Phosphotransferase does not efficiently recognize GAA as lysosomal enzyme
- M6P is critical for the proper binding to M6P receptor and uptake of GAA into target cells

Only Tiny Amounts of rhGAA from Circulation Actually Reach Intended Muscles

Biodistribution of rhGAA ERT to intended muscles is very poor which necessitates highly effi cellular uptake mechanisms



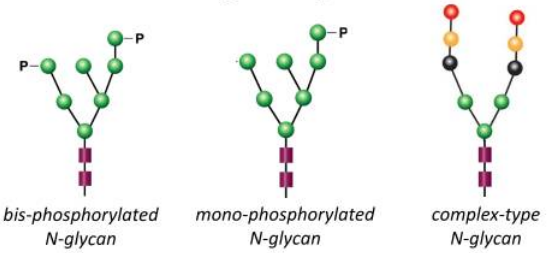
- Relatively high levels of rhGAA ERT can be attain blood after dosing, but only tiny amounts actua reach intended tissues and cells
  - *Only ~1% of rhGAA in blood actually reaches muscle*
  - Mostly cleared by liver, spleen, gut, lymphatic syste
- Resultant rhGAA protein concentrations in the interstitial (outside of target muscle cells) are typically in ***low nanomolar*** range
- At such low protein concentrations, highly effici receptor-mediated uptake of rhGAA ERT is nee for internalization in muscles

N-Glycan Structures Dictate Cellular Uptake of ERTs in Target Cells

Adapted from Tong et al., 1989

Soluble lysosomal enzymes require M6P for cellular uptake; bis-phosphorylated N-glycans w be needed for uptake at low enzyme concentrations

N-Glycan Structures and Binding Affinity for CI-MPR



bis-phosphorylated N-glycan | *mono-phosphorylated N-glycan* | *complex-type N-glycan*

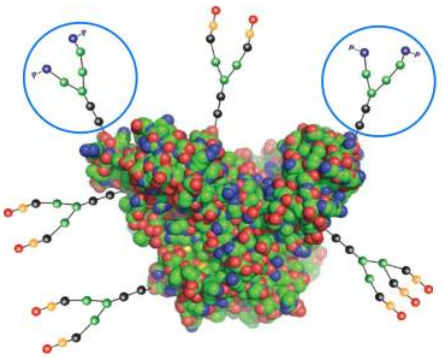
Ligand	Binding affinity (Apparent K_D; nM)*
bis-phosphorylated N-glycan	2
mono-phosphorylated N-glycan	>6000
complex type N-glycan	No binding

**** Low K_D reflects high binding affinity***

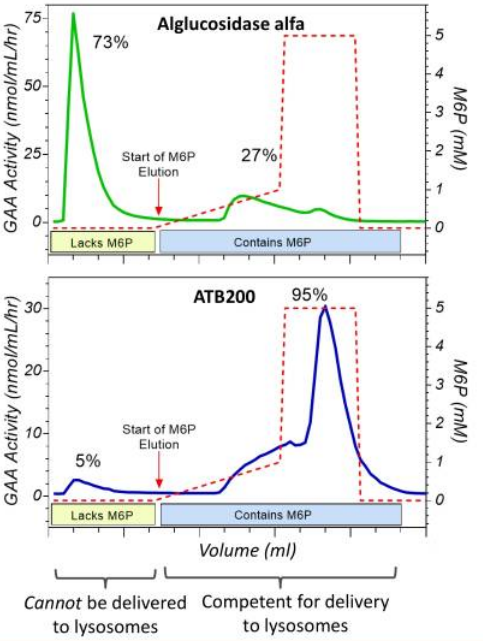
- Bis-phosphorylated N-glycan (2 M6Ps on same N-gly has high affinity for CI-MPR
- Mono-phosphorylated N-glycan has ~3000X lower affinity for CI-MPR
- Complex-type N-glycans do *NOT* bind CI-MPR
- Resultant plasma C_{max} of alglucosidase alfa post-dos 20 mg/kg is ~3400 nM (alglucosidase alfa EPAR prod insert); interstitial concentrations is estimated to be 30-40 nanomolar range
- At low nanomolar enzyme concentrations, only enzy with bis-phosphorylated N-glycans would be able to CI-MPR and internalized in target cells
- Only ~1% of alglucosidase alfa contains bis-phosphorylated N-glycans (Park et al., 2018)

ATB200: Amicus' Optimized rhGAA ERT Has Substantially Higher Binding Affinity to M6P Receptor for Improved Cellular Uptake

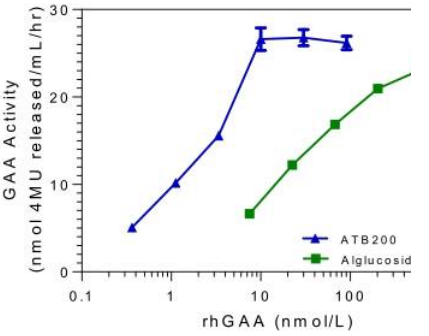
ATB200: Amicus' Next-Generation rhGAA ERT for Pompe Disease



M6P Receptor Chromatography



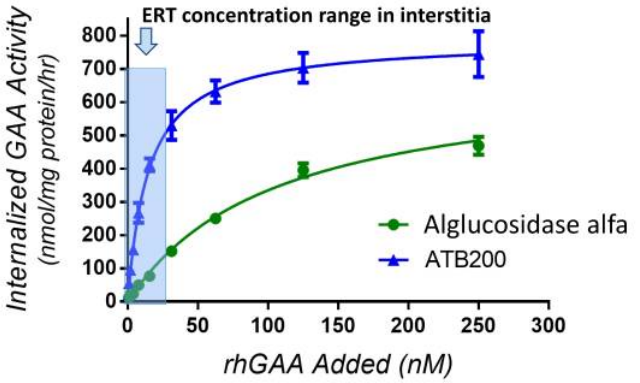
rhGAA Binding Affinity for M6P Re



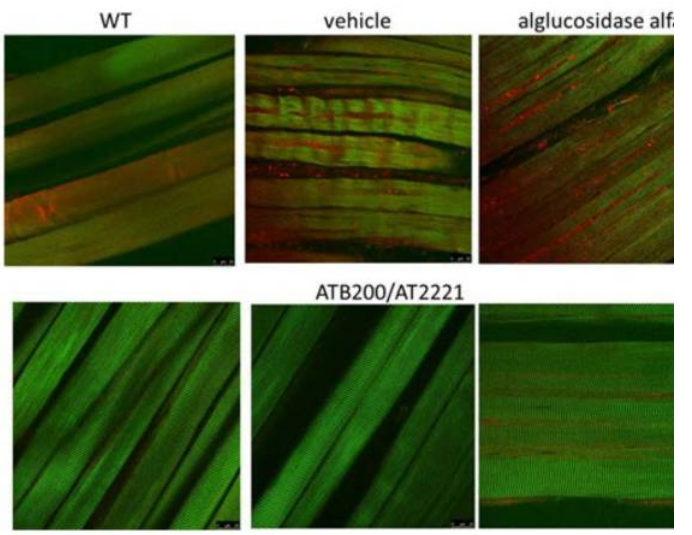
	Apparent K_D (nM)
Alglucosidase alfa	>150
ATB200	2-4

Enhanced Cellular Uptake of AT-GAA Leads to Much Improved Glycogen Reduction and Reversal of Muscle Pathology in Preclinical Models - Xu et al.,

rhGAA Uptake in Skeletal Muscle Myoblasts



Myofiber Structure Analysis by SHG/2PEF Microscopy

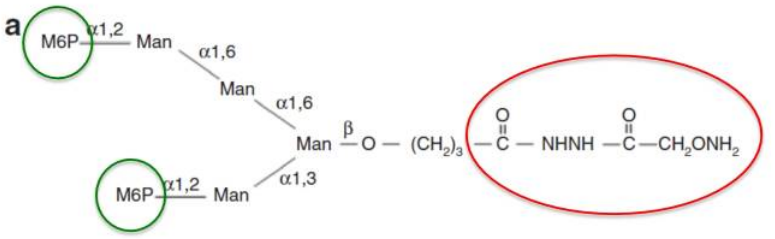


NeoGAA

Key Reported Features of NeoGAA

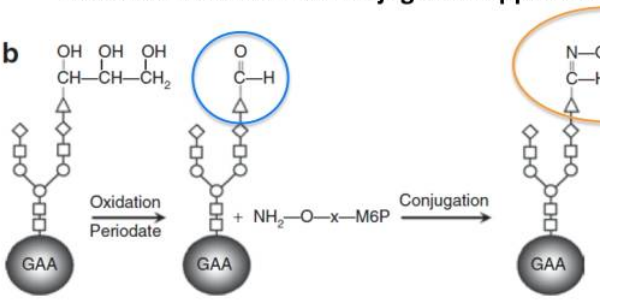
Zhu et al., 2009

Chemical Structure of NeoGlycan



Zhu et al., 2009

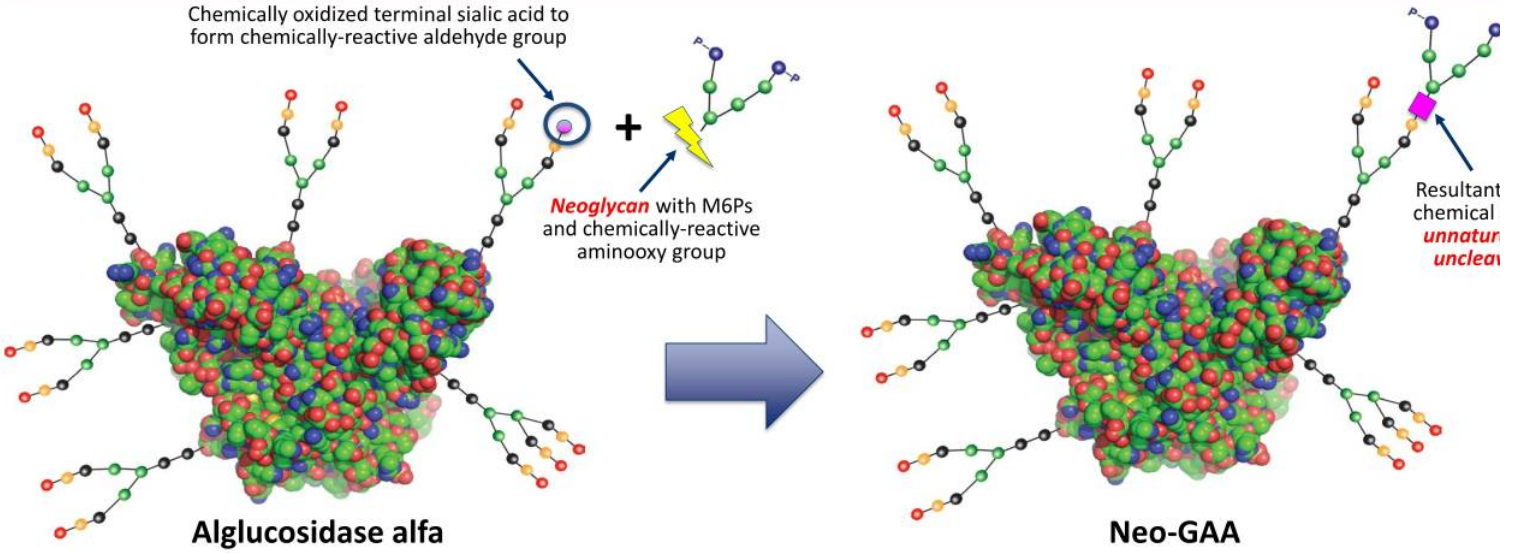
Schematic of Chemical Conjugation Approach



- NeoGAA approach relies upon the chemical conjugation of synthetic M6P-bearing carbohydrate structure (glycan) onto existing N-glycans of alglucosidase alfa to increase M6P content
- Neo-glycan synthesized with chemically reactive aminooxy moiety (red oval) to enable conjugation
- Terminal sialic acids on existing N-glycans are chemically oxidized to form aldehyde structures (blue circle) t serve as acceptors for Neoglycan
- Resultant chemical linkage is a very stable oxime bond (orange oval)

Neo-GAA's Approach for Increasing M6P Levels on Alglucosidase Alfa by Attaching Synthetic Carbohydrate Structure - Zhu et al. 2009

Resultant stable oxime chemical bond is *unnatural and cannot be hydrolyzed* by enzymes wi cells which would negatively impact GAA processing



Schematic based on Zhu et al. 2009

GAA Processing in Lysosomes is Required for Optimal Glycogen Hydrol

Acid α-glucosidase (GAA) is a lysosomal enzyme that hydrolyzes glycogen to glucose. Deficiency of GAA causes Pompe disease. Mammalian GAA is synthesized as a precursor of ~110,000 Da that is *N*-glycosylated and targeted to the lysosome via the M6P receptors. In the lysosome, human GAA is sequentially processed by proteases to polypeptides of 76-, 19.4-, and 3.9-kDa that remain associated. Further cleavage between R^{200} and A^{204} inefficiently converts the 76-kDa polypeptide to the mature 70-kDa form with an additional 10.4-kDa polypeptide. GAA maturation increases its affinity for glycogen by 7–10 fold. In contrast to human GAA, processing of bovine and hamster GAA to the 70-kDa form is more rapid. A comparison of se-

Moreland et al. (2012) *Gene* **491** 25-30

TABLE II

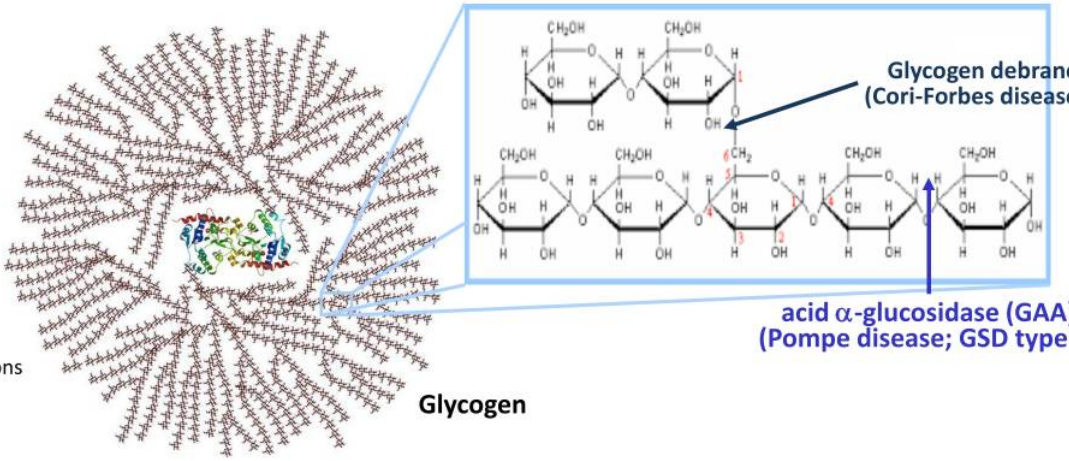
Relation between maturation and glycogen degrading activity of acid α-glucosidase

For each of the molecular forms of acid α-glucosidase the activity for both the natural (glycogen) and the artificial substrate (4-methylumbelliferyl-α-D-glucopyranoside; 4-MU) was measured and the ratio of the activity for glycogen over 4-MU was calculated.

Molecular form	Ratio
110-kDa	1.5
95-kDa	5.2
76/70-kDa	10.7

Wisselaar et al. (1993) *J. Biol. Chem.* **268**(3) 2223-2231

Fully Processed GAA and Debranching Enzyme Are Required for Efficient Glycogen Catabolism in Lysosomes



Public domain images
from WikiMedia Commons

- Glycogen is a large polymer of branched linear glucose chains; GAA and debrancher enzyme involved in degradation
  - GAA primarily hydrolyzes linear α-1,4 glycosidic bonds; has minor activity for α-1,6 glycosidic bonds at branch points
  - Debranching enzyme hydrolyzes α-1,6 glycosidic bonds to release linear fragments at branch points; has transferase activity to add released fragment to extend terminal linear chains
- Unprocessed rhGAA has much lower binding (>*Km*) to glycogen → normal activity for small substrates but lower activi glycogen

ATB200-02 Clinical Outcome in 4 Naive Patients - Behind the Data

Dr Drago Bratkovic MBBS FRACP
Women's and Children's Hospital, Adelaide, South Australia

Government of South Australia
SA Health

Women's & Children's Hospital

Amicus Therapeutics

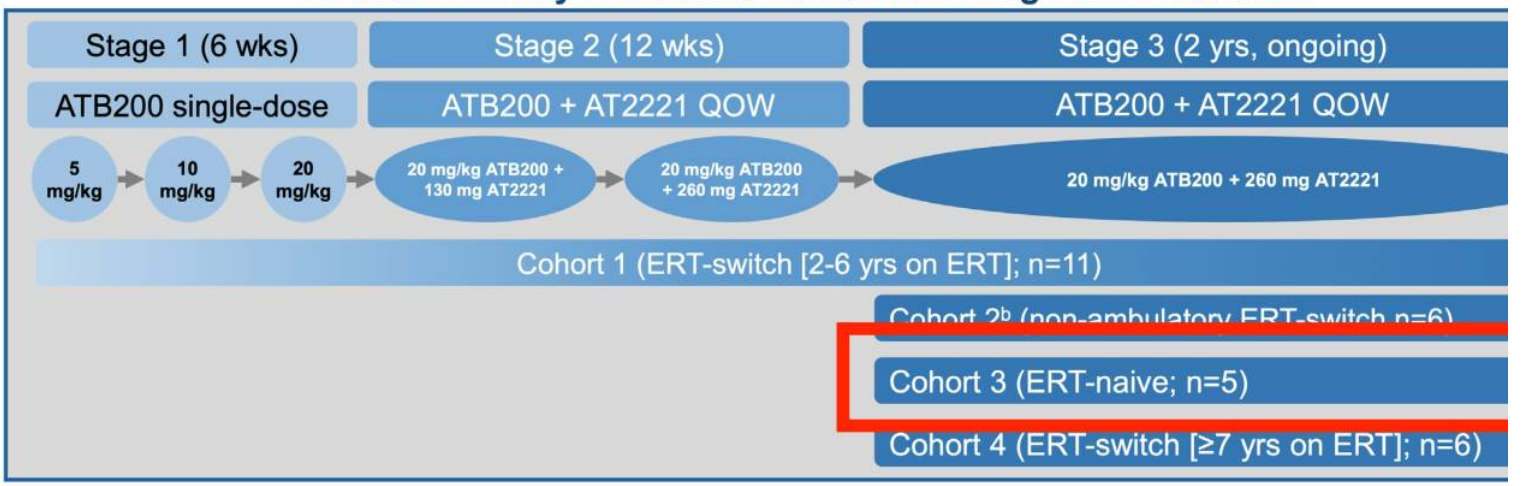
Overview

- ATB200-02 Trial Protocol Overview
- Combined Data
- Individualised Data of Naive Patients
  - 6MWT, FVC, GSGC (Gait, Stair, Gower's, Chair)
  - Patient Reported Outcomes - Fatigue Severity Score
- Clinical Description
- Summary

ATB200-02 Study Design (NCT02675465)

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

18-Week Primary Treatment Period With Long-Term Extension



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

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 ERT-Swi (≥7 yrs on n=6
Age, years, mean (min, max)	**49.4** (28, 66)	**41.5** (18, 57)	**49.4** (24, 65)	**40.8** (20,
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.
6MWT, meters, mean (SD)	**392.0** (93.4)	NA	**399.5** (83.5)	**387.3 (16**
Upright FVC, % predicted, mean (SD)	**52.3** (13.2)	42.3 (28.2)[b]	**53.3** (20.4)	**65.3 (21.**

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)	
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)	
3	ERT-Naive	**399.5** (83.5)	5	**+41.8** (29.4)	5	**+63.1** (29.1)	5	**+60.7** (36.5)	

- 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 patie

Cohort		Baseline		Change From Baseline				
				Month 6		Month 12		Month 24
		mean (SD)	n	mean (SD)	N	mean (SD)	n	mean (SD)
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)
3	ERT-Naive	**53.2** (20.1)	5	**+4.4** (5.6)	5	**+4.6** (8.8)	5	**+6.8** (6.8)

- 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.

GSGC

Combination of:

- Gait (G)
- Climbing stairs (S)
- Gower's maneuver (G)
- Arising from a chair (C)

Quality of the activity is scored by an observer and timed

Measure of day to day activities

Scored as the sum of the scores

- Lower the better
- Maximum 27, Minimum 4

Table 1. The GSGC score.

Gait (G)
1-normal
2-Mild waddling, lordosis, and/or toe walking
3-Moderate waddling, lordosis, and/or toe walking
4-Severe waddling, lordosis, and/or toe walking
5-Walks only with assistance (i.e., braces, cane, crutches)
6-Stands, but unable to walk
7-Confined to wheelchair
Time to walk 10 meters: _____seconds

Climbing stairs (S)
1-Climbs without assistance
2-Supports one hand on thigh
3-Supports both hands on thighs
4-Climb stairs in upright position but with aid of railing
5-Climbs while clinging to the railing with both hands
6-Manages to climb only a few steps
7-Unable to climb steps
Time to climb steps: _____seconds

Gower's maneuver (G)
1-Normal
2-Butt-first maneuver, one hand on floor
3-Butt-first maneuver, two hands on floor
4-Unilateral hand support on thigh
5-Bilateral hand support on thighs
6-Arises only with aid of an object (table, chair, etc.)
7-Unable to arise
Time to standing from sitting: _____seconds

Arising from a chair (C)
1-Normal
2-With wide base and/or difficulty, but without support
3-With support on one thigh
4-With support on both thighs
5-With support on arms of chair or on a table
6-Not possible
Time to standing from sitting: _____seconds

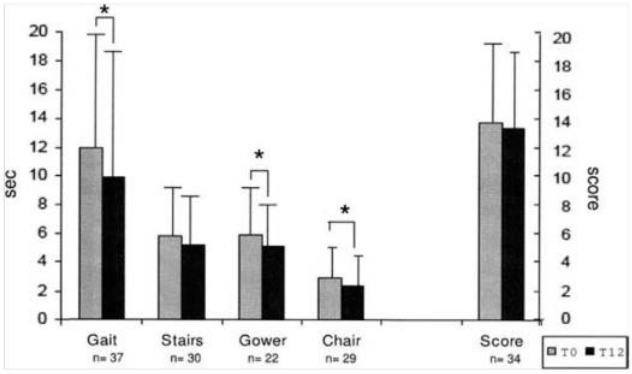


FIGURE 1. Results of the GSGC score before and after 1 year of ERT. T0 = baseline. T12 = 12 months. The functional tests are timed in seconds, while the score expresses the sum of points of each test. Asterisks show significance $P < 0.05$.

NEW MOTOR OUTCOME FUNCTION MEASURES IN EVALUATION OF LATE-ONSET POMPE DISEASE BEFORE AND AFTER ENZYME REPLACEMENT THERAPY

CORRADO ANGELINI, MD,[1,2] CLAUDIO SEMPLICINI, MD,[1] SABRINA RAVAGLIA, MD,[3,4] MAURIZIO MOGGIO, MD,[5] GIACOMO P. COMI, MD,[5] OLIMPIA MUSUMECI, MD,[6] ELENA PEGORARO, MD,[1] PAOLA TONIN, MD,[7] MASSIMILIANO FILOSTO, MD,[8] SERENELLA SERVIDEI, MD,[9] LUCIA MORANDI, MD,[10] GRAZIA CRESCIMANNO, MD,[11] GIOVANNI MARROSU, MD,[12] GABRIELE SICILIANO, MD,[13] TIZIANA MONGINI, MD,[14] and ANTONIO TOSCANO, MD[6] and the Italian Group on GSDII

Timed Motor Function Tests

Timed motor function test results improved for both ERT-switch ambulatory and ERT-nai 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
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.
		GSGC Score	**12.6** (4.8)	**+0.1** (3.9)	**−0.3** (4.1)	**-0.1** (5.
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.
		GSGC Score	**12.2** (3.6)	**−1.8** (3.8)	**−0.8** (2.5)	**-1.8** (2.

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 2
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 (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

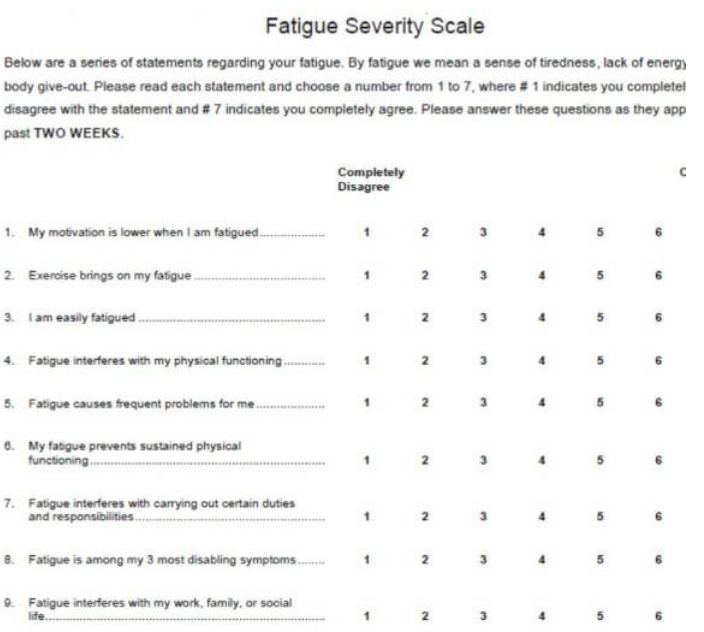
7 point scale

9 questions

Range 7 to 63

- Sometimes expressed as a mean of the 9 scores (1-7)
- Lower the Better

Validated and used in a number of neurological disorders including Pompe disease



Fatigue Severity Scale

Below are a series of statements regarding your fatigue. By fatigue we mean a sense of tiredness, lack of energy body give-out. Please read each statement and choose a number from 1 to 7, where # 1 indicates you completel disagree with the statement and # 7 indicates you completely agree. Please answer these questions as they app past **TWO WEEKS**.

	Completely Disagree					C
1. My motivation is lower when I am fatigued	1	2	3	4	5	6
2. Exercise brings on my fatigue	1	2	3	4	5	6
3. I am easily fatigued	1	2	3	4	5	6
4. Fatigue interferes with my physical functioning	1	2	3	4	5	6
5. Fatigue causes frequent problems for me	1	2	3	4	5	6
6. My fatigue prevents sustained physical functioning	1	2	3	4	5	6
7. Fatigue interferes with carrying out certain duties and responsibilities	1	2	3	4	5	6
8. Fatigue is among my 3 most disabling symptoms	1	2	3	4	5	6
9. Fatigue interferes with my work, family, or social life	1	2	3	4	5	6

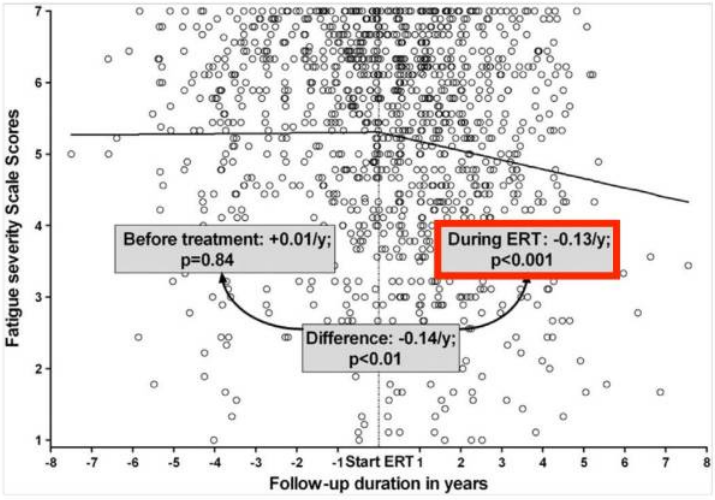


Fig. 1. The figure shows the change in Fatigue Severity-Scale scores (FSS) before and after the start of enzyme replacement therapy (ERT). The dots represent individual measurements and the lines represent the mean slopes calculated by the 'broken stick' repeated measures ANOVA for the group of 163 patients. The median follow-up during the natural course of Pompe disease was 4 years and the median follow-up during treatment was 3 years. The mean FSS score did not change significantly in the period before ERT, but declined significantly during ERT. The difference between the period before and during ERT was 0.14 FSS score points per year ($p < 0.01$).

Enzyme replacement therapy and fatigue in adults with Pompe disease

Deniz Güngör [a], Juna M. de Vries [b], Esther Brusse [b], Michelle E. Kruijshaar [a], Wim C.J. Hop [d], Magda Murawska [d], Linda E.M. van den Berg [a], Arnold J.J. Reuser [c], Pieter A. van Doorn [b], Marloes L.C. Hagemans [a], Iris Plug [a], Ans T. van der Ploeg [a,*]

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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)	
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)	
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)	
3	ERT-Naive	**39.2** (12.7)	5	**-5.2** (11.7)	5	**-7.2** (7.5)	5	**-7.2** (11.9)	

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 patie
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 e
fatigue. The normative value in the healthy population is ~27.[1]

Data from interim analysis 8.

Subject 1

Early 40s and mother of 2 pre teen children

Diagnosed 4 years prior to ATB200-02

Noticing gradual decline in motor function especially in last few years

Unable to safely run and requiring support to get up stairs

Not on BiPAP and minimal other health issues

Since commencing AT-GAA

- Not seen any decline in her physical skills
- Back to exercising regularly and seeing an increase in her muscle bulk
- More able to take an active part of her children's school and sport
- All of this has helped greatly with her mentally and she feels stronger and more resilient
- Considering going back to work!

	Baseline	Change at 12 months	Change 24 mont
6MWT (m)	480	94.6	78.2
FVC %	69	12	9
GSGC (4-27)	9	1	-2
FSS (1-7)	2.6	-0.3	0.9

Subject 2

Mid 20's and living at home with her mother

Diagnosed 5 years prior to study with issues getting up from a chair and increasing headaches. GP noticed a positive Gower's sign

Significant respiratory compromise

- BiPAP overnight and 2-4 hours during the day
- FVC 32%
- Unable to lay flat

Less motor compromise when compared to respiratory issues

Since Commencing AT-GAA

- Has ceased use of BiPAP during the day
- Now able to lay flat and speak on the phone
- Able to walk up hills she was previously unable to do
- In last 6 months has started part time work

	Baseline	Change at 12 months	Change 24 mont
6MWT (m)	384.1	78.9	106.9
FVC %	32	1	-2
GSGC (4-27)	10	-1	-4
FSS (1-7)	5.3	0.0	-0.9

Subject 3

Early 60's

Symptomatic from 40's similar to her sister who was diagnosed at this age.

Put off testing until she started having problems with her sleep and headaches

Relatively intact upper limb strength

BiPAP overnight but nil during the day

Since commencing AT-GAA

- Developed mild cardiac failure within the first few months of starting ERT - easily managed with diuretics
- Able to complete housework without needing to rest
- Improved sleep and energy levels
- Now can lay flat without immediately becoming short of breath
- More stable gait and reduction in falls

	Baseline	Change at 12 months	Change 24 mont
6MWT (m)	267.3	30.8	20.7
FVC %	48	13	16
GSGC (4-27)	18	0	1
FSS (1-7)	4.3	-1.3	-1.3

Subject 4

Female, Mid 60's

Initially diagnosed with a limb-girdle muscular dystrophy in late 50's. Eventually tested for Pompe disease.

Unable to pick up grandchildren and trouble keeping up with her husband on walks

No BiPAP or respiratory problems

Since Commencing AT-GAA

- Now able to walk further and keep up with her husband
- Not the degenerative disease that she was told she would have
- Feels no different to other people her age
- Overall more energy

	Baseline	Change at 12 months	Change 24 mont
6MWT (m)	406.3	33.4	26.4
FVC %	79	7	8
GSGC (4-27)	11	1	0
FSS (1-7)	3.3	-2.0	-2.3

Compassionate Access Single Case Review

John F. Crowley, Chairman and Chief Executive Officer
Markus Peceny, Medical Director

Expanded Access Program (EAP) Request

Amicus received the compassionate use request on 24th September 2019

"This is a request for emergency early access to your new acid glucosidase preparation that has a higher amount of mannose-6-phosphate residues and is combined with miglustat for enzyme stabilization. [...]

My request is for a 14 months old boy with severe, CRIM-negative infantile Pompe disease. He is on Myozyme therapy since February. Current dose is 40 mg/kg b.w./week, i.e. 4 times the recommended dose. [...] He received an immunmodulation (sic) with rituximab and methotrexate prior to therapy initiation and has no antibodies versus acid glucosidase. Nevertheless, his response to treatment has been poor. Cardiomyopathy was hardly influenced, and cardiac function is limited (FS 10-20%).

We expect the patient to die from disease complications if the treatment cannot be improved. [...] With your help, he will at least have a fair chance."

EAP Request

EAP Request

A Message from the Parents

EAP Request Granted

Amicus early access granted on 4th October 2019

"God bless you all for your incredible work and your positive decision. I am sure you have saved a life here!!!

THANK YOU!!!!!!!!!!!!!!!!!!!!!!!!!!!!

I am in pediatric metabolic diseases for more than 25 years now, I can't remember any situation where a team has put so much heart (and work) into saving a child …Will inform the parents immediately, they haven't slept for days…"

Diagnosis, Treatment History and Initiation of AT-GAA

IOPD CRIM-negative infant initiated treatment on alglucosidase alfa at 7 months of age; experienced decline in cardiac function even after going to 40mg/week. Improved on AT-GA

Diagnosis

- Diagnosis of IOPD Jan 2019 (6.5 months old) based on incidental finding of cardiomegaly during respiratory infection
- At the time of diagnosis he presented with hypertrophic cardiomyopathy and hypotonia

SoC Treatment

- Alglucosidase alfa initiated on 14th Feb 2019 @ labelled dose of 20 mg/kg once every two weeks *
- On alglucosidase alfa: progressive decline in cardiac function; fractional shortening (FS) decreased from 21% to 9%
- Dose of alglucosidase alfa increased on 14th May 2019 to 40 mg/kg once every week (4 times approved dose)
  - Initial improvement in cardiac function (FS increased from 9% to 21%) followed by progressive worsening to the point of FS being unmeasurable

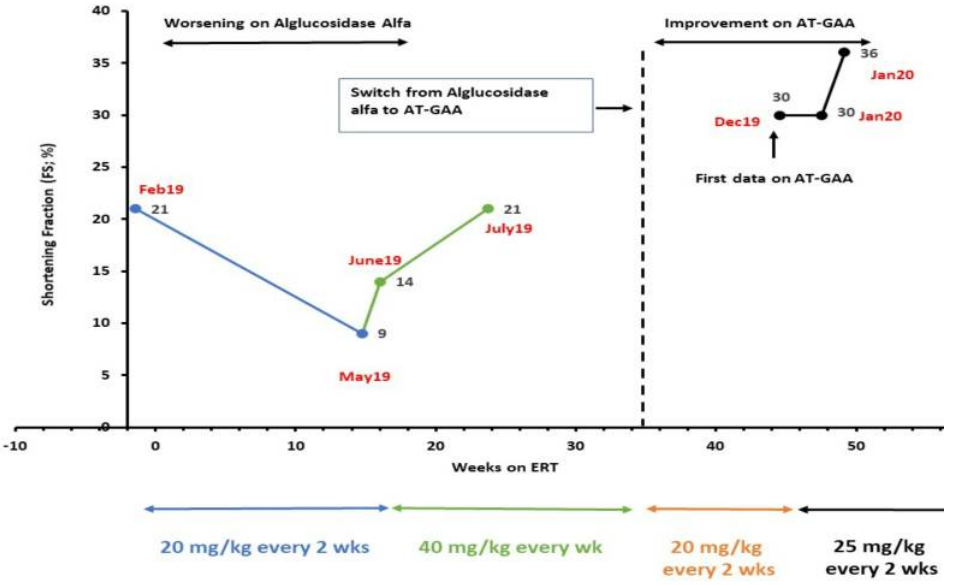
AT-GAA Treatment

- Initiated AT-GAA on 15th Oct 2019 at 20 mg/kg every other week
  - Significant improvement in cardiac function with increase in FS to 30%; motor function improved
- Increased dose of AT-GAA on 23rd Dec 2019 to 25 mg/kg every other week
  - Additional improvement in cardiac function with increase in FS to 36%; motor function improved, and supplemental oxygen no longer required

** Patient was immunomodulated with rituximab and methotrexate prior to initiating alglucosidase alfa to limit antibody formation*

Clinical Response to ERT measured via Fractional Shortening (FS)

After switching to AT-GAA the fractional shortening improved from unmeasurable to a value of 30-36% after only 2-3 months; motor function improved and supplemental oxygen no longer required



Prof. Marquart's Video Testimony

Parent Video Testimony

Thank You

Amicu
Therapeut