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

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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, 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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