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

October 2, 2019

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

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

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

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

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

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

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

Dr. Schoser stated, "There is a clear need for a new treatment option to address multiple aspects of Pompe disease across a broad spectrum of Pompe patients, including previously untreated and ERT-switch patients as well as non-ambulatory patients. The twenty four month results from this Phase 1/2 clinical study of AT-GAA continue to demonstrate a robust effect in adult people living with Pompe disease, including improvements in six minute walk distance among ambulatory ERT-switch and ERT-naïve participants and sustained positive changes in arm and shoulder strength among the non-ambulatory ERT-switch patients. These new data in the Cohort 4 patients are particularly impressive showing the potential for AT-GAA to change the course of the disease in these patients. I look forward to continuing to follow patients from this Phase 2 study in addition to the ongoing PROPEL pivotal study."

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

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

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

- **Motor function:** Six-minute walk test (6MWT), a primary measure of motor function in Pompe disease patients, improved in both ERT-naive and ERT-switch patients with continued benefit observed out to month 24. Improvements were generally consistent across both cohorts.
    - All 5 ERT-naive patients showed increases in 6MWT distance at all time points out to month 24. The ERT-naïve patients showed mean increases of 42 meters at month 6 (n=5), 63 meters at month 12 (n=5), and 61 meters at month 24 (n=5).

- 6MWT increased in 7/10, 9/10, and 8/9 ERT-switch patients in Cohort 1 at Months 6, 12, and 24 respectively. The ERT-switch patients in Cohort 1 showed mean increases of 24 meters at month 6 (n=10), 42 meters at month 12 (n=10), and 36 meters at month 24 (n=9).

- Other motor function tests generally showed mean improvements consistent with 6MWT distance out to month 24 in all ambulatory cohorts.

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

- **Pulmonary Function:** Pulmonary function improved in ERT-naïve patients and was generally stable in ERT-switch patients.

    - In ERT-naïve patients, mean absolute change in forced vital capacity (FVC), one of the main measures of pulmonary function in Pompe disease, was +4.2% at month 6 (n=5), +4.5% at month 12 (n=5), and +6.8% at month 24 (n=5).

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

    - Overall, other pulmonary tests of maximal inspiratory pressure (MIP), a measure of inhalation, and maximal expiratory pressure (MEP), a measure of exhalation, were stable or increased in both ERT-naïve and ERT-switch patients across all cohorts.

Cohort 4 (n=6)

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

- **Motor Function**: Muscle function improved in 2/5 patients at month 6 and 4/6 patients at the last available time point:

    - Historical data on 6MWT for the six patients showed an average decline of approximately 7 meters per year while on standard of care ERT prior to switching to AT-GAA (n=6), with 5/6 patients declining.

    - After switching to AT-GAA, the patients in Cohort 4 showed mean increases of 24 meters at month 6 (n=5) and 19 meters at their last available timepoint (n=6). 6MWT increased in 2/5 patients at month 6 and 4/6 patients at the last available time point.

    - Other motor function tests generally showed mean improvements consistent with 6MWT distance at month 6 (n=5) and at their last available timepoint (n=6).

    - All patients showed improvements in strength testing from baseline to month 6 and at the last available timepoint, as measured by quantitative muscle testing (QMT) and manual muscle testing (MMT).

- **Pulmonary Function**: Pulmonary function improved at month 6 (n=5) and at the last available time point (n=6).
    - After switching to AT-GAA, FVC increased in 5/6 patients at month 6 and 5/6 patients at the last available time point. Mean absolute change in FVC was +6.6% at month 6 (n=5) and +5.2% at the last available time point (n=6).
    - Overall, other pulmonary tests of maximal inspiratory pressure (MIP), a measure of inhalation, and maximal expiratory pressure (MEP), a measure of exhalation, were stable or increased in all patients at month 6 (n=5) and at the last available timepoint (n=6).

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

- Safety and tolerability data reflect a maximum of 40 months of treatment. To date, adverse events have been generally mild and transient.
- AT-GAA has resulted in a low rate of infusion-associated reactions (IARs) following 1,500+ infusions (28 incidents of IARs in 8 patients; 1.8% of all 1,500+ infusions with an IAR).
- The clinical pharmacokinetic profile has been consistent with previously reported preclinical data.
- Persistent and durable reductions in key biomarkers of muscle damage (creatine kinase, or CK) and disease substrate (urine hexose tetrasaccharide, or Hex4) across all patient cohorts out to month 24 continue to suggest a positive effect on muscle tissue.
- Anti-GAA antibodies were observed in the majority of Cohort 1 and Cohort 3 patients from baseline to month 24. There was no impact of antibodies on safety, efficacy and exposure or clearance of ATB200. Data on impact of antibodies for Cohorts 2 and 4 are not currently available.

AT-GAA Development and Regulatory Strategy
The Company's strategy is to enhance the body of clinical data for AT-GAA in ongoing clinical studies, including the pivotal study (PROPEL, also referred to as ATB200-03) to deliver this potential new therapy to as many people living with Pompe disease as soon as possible. Based on feedback from US and EU regulatory authorities, Amicus expects the PROPEL study to support approval for a broad indication, including ERT-switch and treatment-naïve patients.

Anticipated Pompe Milestones:

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

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

About ATB200-02 Clinical Study
The primary objectives of the open-label ATB200-02 clinical study are to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of ATB200/AT2221 over an 18-week primary treatment period followed by a long-term extension. Sixteen clinical sites in five countries participated in the ATB200-02 clinical study. The study originally enrolled a total of 20 patients across three patient cohorts: ambulatory ERT-experienced (Cohort 1, n=11), non-ambulatory ERT-experienced (Cohort 2, n=4) and ERT-naïve (Cohort 3, n=5); in addition two more patients were enrolled in cohort 2. A fourth cohort of 6 ambulatory ERT-switch patients was also been enrolled, adding to the patient data in the ambulatory ERT-switch population. Patients in Cohort 1 received escalating doses of ATB200 (5, 10, 20 mg/kg), followed by 3 doses of 20 mg/kg ATB200 plus low dose AT2221, followed by ongoing doses of 20 mg/kg ATB200 plus high dose AT2221. Patients in Cohorts 2, 3, and 4 all receive 20 mg/kg ATB200 plus high dose AT2221.

About AT-GAA
AT-GAA is an investigational therapy that consists of ATB200, a unique recombinant human acid alpha-glucosidase (rhGAA) enzyme with optimized carbohydrate structures, particularly mannose-6 phosphate (M6P), to enhance uptake, co-administered with AT2221, a pharmacological chaperone. In preclinical studies, AT-GAA was associated with increased tissue enzyme levels, reduced glycogen levels in muscle, and improvements in muscle strength. A global Phase 1/2 study (ATB200-02) is ongoing to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics of AT-GAA.

Amicus has also initiated a global Phase 3 clinical study (ATB200-03, or PROPEL) of AT-GAA in adult patients with late onset Pompe disease. PROPEL is a 52-week, double-blind randomized study designed to assess the efficacy, safety and tolerability of AT-GAA compared to the current standard of care, alglucosidase alfa, an enzyme replacement therapy (ERT). More information, including a list of participating sites, is available at www.clinicaltrials.gov: NCT03729362.

About Pompe Disease
Pompe disease is an inherited lysosomal storage disorder caused by deficiency of the enzyme acid alpha-glucosidase (GAA). Reduced or absent levels of GAA leads to accumulation of glycogen in cells, which is believed to result in the clinical manifestations of Pompe disease. The disease can be debilitating, and is characterized by severe muscle weakness that worsens over time. Pompe disease ranges from a rapidly fatal infantile form with significant impacts to heart function to a more slowly progressive, late-onset form primarily affecting skeletal muscle. It is estimated that Pompe disease affects approximately 5,000 to 10,000 people worldwide.

About Amicus Therapeutics
Amicus Therapeutics (Nasdaq: FOLD) is a global, patient-dedicated biotechnology company focused on discovering, developing and delivering novel high-quality medicines for people living with rare metabolic diseases. With extraordinary patient focus, Amicus Therapeutics is committed to advancing and expanding a robust pipeline of cutting-edge, first- or best-in-class medicines for rare metabolic diseases. For more information please visit the company's website at www.amicusrx.com, and follow us on Twitter and LinkedIn.

Forward-Looking Statements
This press release contains "forward- looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements relating to preliminary data from a global Phase 1/2 study to investigate AT-GAA for the treatment of Pompe and the potential implications on these data for the future advancement and development of AT-GAA. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "confidence," "encouraged," "potential," "plan," "targets," "likely," "may," "will," "would," "should" and "could," and similar expressions or words identify forward-looking statements. The forward looking statements included in this press release are based on management's current expectations and belief's which are subject to a number of risks, uncertainties and factors, including that the preliminary data based on a small patient sample and reported before completion of the study will not be predictive of future results, that results of additional preliminary data or data from the completed study or any future study will not yield results that are consistent with the preliminary data presented, that the Company will be not able to demonstrate the safety and efficacy of AT-GAA, that later study results will not support further development, or even if such later results are favorable, that the Company will not be able to successfully complete the development of, obtain regulatory approval for, or successfully commercialize AT-GAA. In addition, all forward looking statements are subject to the other risks and uncertainties detailed in our Annual Report on Form 10-K for the year ended December 31, 2018 and Quarterly Report on 10-Q for the Quarter ended June 30, 2019. As a consequence, actual results may differ materially from those set forth in this press release. You are cautioned not to place undue reliance on these forward looking statements, which speak only of the date hereof. All forward looking statements are qualified in their entirety by this cautionary statement and we undertake no obligation to revise this press release to reflect events or circumstances after the date hereof.

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