New 4-Year Data for Pombiliti® (cipaglucosidase alfa-atga) + Opfolda® (miglustat) Presented at ICIEM

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Long-Term Data Adds to the Growing Body of Evidence Supporting the Compelling Clinical Profile of Pombiliti® + Opfolda®

PRINCETON, N.J., Sept. 08, 2025 (GLOBE NEWSWIRE) -- Amicus Therapeutics (Nasdaq: FOLD), today announced the presentation of new 4-year muscle function, muscle strength and biomarker endpoints from the PROPEL open-label extension (OLE) study of cipaglucosidase alfa-atga + miglustat (cipa+mig) in adults with late-onset Pompe disease (LOPD) at the International Congress of Inborn Errors of Metabolism (ICIEM) in Kyoto, Japan.

The new analysis, “208-week efficacy and safety of cipaglucosidase alfa plus miglustat in patients with late-onset Pompe disease treated from PROPEL baseline: muscle function and biomarkers,” was conducted on the 82 patients (62 ERT-experienced and 20 ERT-naïve) who were randomized to cipa+mig in PROPEL and who enrolled in the open label extension (OLE).

Pombiliti + Opfolda is indicated in the U.S. for the treatment of adult patients with LOPD weighing ≥40 kg and who are not improving on their current ERT. In the U.S., Pombiliti + Opfolda is not indicated for patients naïve to ERT treatment. The data summarized below are from the ERT-experienced group in the OLE. Pulmonary function data from the PROPEL OLE will be presented separately at an upcoming conference.

The mean age was 48.8 years and the median duration of prior ERT in the ERT-experienced cohort at PROPEL baseline was 7.5 years. In the ERT-experienced group, the measures of muscle function, muscle strength and biomarkers improved and/or were sustained out to 208 weeks. Mean change from PROPEL baseline to week 208 were as follows:

- Percent predicted six-minute walk distance (6MWD), +2.3%;
- Lower extremity manual muscle test (MMT) score, +1.6 points;
- Gait-Stairs-Gowers-Chair (GSGC) score, +0.1 points;
- PROMIS® physical function score, +1.2 points;
- Serum creatine kinase (CK) levels, -160.0 serum CK; and,
- Urine hexose tetrasaccharide (Hex4), -1.9 mmol/mol creatinine.

No new safety signals were identified. Up to week 208, 41 patients experienced treatment-related treatment-emergent adverse events (TEAEs), leading to four cipa+mig discontinuations, and two patients experienced serious treatment-related TEAEs, leading to two cipa+mig discontinuations. One patient experienced a TEAE (worsening of Lewy body disease) unrelated to study treatment, which led to death; the patient had discontinued from the study prior to death.

“Durability of effect is important for evaluating the impact of treatments for individuals with LOPD. In this new analysis assessing the long-term outcomes from the open label extension of PROPEL, the improvements in muscle function, muscle strength, and biomarkers observed in patients receiving Pombiliti and Opfolda were maintained for four years,” said Priya Kishnani, MD, Chief, Division of Medical Genetics, Chen Family Distinguished Professor of Pediatrics, Chief, Division of Medical Genetics, Duke University Medical Center.

“This new analysis adds to the growing body of evidence supporting the compelling clinical profile of Pombiliti and Opfolda in ERT-experienced adults,” said Jeff Castelli, PhD, Chief Development Officer, Amicus Therapeutics, Inc. “To observe these sustained improvements and stability in the patients in the open label extension at four years is very encouraging given the progressive nature of LOPD. We look forward to presenting long-term extension data across pulmonary measures soon and will continue to closely study Pombiliti and Opfolda as part of our commitment to make a meaningful difference in the lives of people living with late-onset Pompe disease.”

Other abstracts at ICIEM
In addition to this analysis, the following abstracts related to Pombiliti + Opfolda based on Amicus studies were also presented at ICIEM:

Abstract Title: *Cipaglucosidase alfa and alglucosidase alfa enzymes have similar stability at neutral pH and can be stabilized with miglustat*

- **Presenter:** Filip Cosmanescu, Amicus Therapeutics Inc., Princeton, NJ, U.S.A.

Abstract Title: *Integrating clinical evidence on cipaglucosidase alfa plus miglustat and alglucosidase alfa via a multi-level network meta-regression*

- **Presenter:** William Kerr, Amicus Therapeutics Ltd, Marlow, U.K.

Abstract Title: *PROPEL Japan subpopulation: efficacy and safety of cipaglucosidase alfa plus miglustat versus alglucosidase alfa in patients with late-onset Pompe disease*

- **Presenter:** Hiroshi Kobayashi, The Jikei University School of Medicine, Tokyo, Japan

Abstract Title: *ATB200-19: an open-label, expanded access study of the safety and effectiveness of cipaglucosidase alfa plus miglustat in adults with late-onset Pompe disease in Japan*

- **Presenter:** Aya Narita, ISEIKAI International General Hospital, Osaka, Japan

Abstract Title: *PROPEL Australia subpopulation: efficacy and safety of cipaglucosidase alfa plus miglustat versus alglucosidase alfa in patients with late-onset Pompe disease*

- **Presenter:** Michel Tchan, Westmead Hospital, Westmead, NSW, Australia

The following abstract related to Pombiliti + Opfolda from a non-Amicus study was also presented at ICIEM:

Abstract Title: *Real World Study: Assessing the impact of switching from alpha-glucosidase to cipaglucosidase alfa with miglustat on disease progression in adults with Pompe disease*

- **Lead author:** Sara Lucas Del Pozo, National Hospital for Neurology and Neurosurgery, UCLH, London, U.K.
- **Presenter:** Robin Lachmann, National Hospital for Neurology and Neurosurgery, UCLH, London, U.K.

About the PROPEL Study
PROPEL was a 52-week, double-blind randomized global study designed to assess the efficacy, safety, and tolerability of cipaglucosidase alfa-atga + miglustat compared to non-U.S. approved alglucosidase alfa + placebo (the comparator). The study enrolled 123 adult LOPD patients who still had the ability to walk and to breathe without mechanical ventilation.

Patients enrolled in PROPEL were randomized 2:1 so that for every two patients randomized to be treated with cipaglucosidase alfa-atga + miglustat, one was randomized to be treated with the comparator. Of the patients enrolled in PROPEL, 77% were being treated with alglucosidase alfa (n=95) for at least 2 years at study entry and 23% had never been treated with any ERT (n=28). 117 of the 123 patients (>95%) completed the PROPEL study.

Efficacy endpoints of the study included primary endpoint of change from baseline to week 52 in 6-minute walk distance (6MWD) for comparison of superiority and key secondary endpoint of change from baseline to week 52 in forced vital capacity (FVC). PROPEL did not achieve statistical significance for the primary endpoint of superiority in change from baseline to week 52 in 6MWD in the overall population. After 52 weeks, ERT-experienced patients treated with cipaglucosidase alfa-atga + miglustat (n=61) walked an estimated 17 meters (95% CI, 0.2, 33) farther than the comparator group (n=29). After 52 weeks, ERT-experienced patients treated with cipaglucosidase alfa-atga + miglustat (n=55) showed an estimated treatment difference of 3.5% (95% CI, 1.0, 6.0) in FVC compared with the comparator group (n=29).

About the PROPEL Open-label Extension Study
The Phase 3 open-label extension (OLE) study (ATB200-07) is a multicenter, international study designed to evaluate the long-term safety and efficacy of cipaglucosidase alfa-atga + miglustat in adult subjects with LOPD who completed the Phase 3 PROPEL Study (ATB200-03). Of the 118 patients treated in the OLE, 81 continued cipa+mig treatment from PROPEL (cipa+mig group; 61 ERT-experienced prior to PROPEL; 20 ERT-naïve) and 37 switched from alg+pbo to cipa+mig (switch group; 29 ERT-experienced; 8 ERT-naive).

Efficacy endpoints of the study included primary endpoint of change from PROPEL baseline to approximately 4 years in 6-minute walk distance (6MWD), forced vital capacity (FVC), creatine kinase (CK) and hexose tetrasaccharide (Hex4) levels, patient-reported outcomes and safety.

About Pombiliti + Opfolda
Pombiliti® + Opfolda®, is a two-component therapy that consists of cipaglucosidase alfa-atga, a bis-M6P-enriched rhGAA that facilitates high-affinity uptake through the M6P receptor while retaining its capacity for processing into the most active form of the enzyme, and the oral enzyme stabilizer, miglustat, that's designed to reduce loss of enzyme activity in the blood.

U.S. INDICATIONS AND USAGE
POMBILITI in combination with OPFOLDA is indicated for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT).

SAFETY INFORMATION

HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS: Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available. If a severe hypersensitivity reaction occurs, POMBILITI should be discontinued immediately and appropriate medical treatment should be initiated. INFUSION-ASSOCIATED REACTIONS (IARs): If severe IARs occur, immediately discontinue POMBILITI and initiate appropriate medical treatment. RISK OF ACUTE CARDIORESPIRATORY FAILURE IN SUSCEPTIBLE PATIENTS: Patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function, may be at risk of serious exacerbation of their cardiac or respiratory status during POMBILITI infusion. See PI for complete Boxed Warning. CONTRAINDICATION: POMBILITI in combination with Opfolda is contraindicated in pregnancy. **EMBRYO-FETAL TOXICITY:** May cause embryo-fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for at least 60 days after the last dose. **Adverse Reactions:** Most common adverse reactions ≥ 5% are headache, diarrhea, fatigue, nausea, abdominal pain, and pyrexia. **Please see full PRESCRIBING INFORMATION, including BOXED WARNING, for POMBILITI (cipaglucosidase alfa-atga) LINK and full PRESCRIBING INFORMATION for OPFOLDA (miglustat) LINK.**

About Late-Onset Pompe Disease
Late-onset Pompe disease is an inherited lysosomal disorder caused by deficiency of the enzyme acid alpha-glucosidase (GAA). Reduced or absent levels of GAA lead to accumulation of glycogen in cells, which is believed to result in the clinical manifestations of Pompe disease. Late-onset Pompe disease can be severe and debilitating with progressive muscle weakness throughout the body that worsens over time, particularly skeletal muscles and muscles that control breathing.

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 diseases. With extraordinary patient focus, Amicus Therapeutics is committed to advancing and expanding a pipeline of cutting-edge, first- or best-in-class medicines for rare diseases. For more information please visit the company's website at www.amicusrx.com, and follow on X and LinkedIn.

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