Amicus Therapeutics Announces Positive Pompe Program Updates

**AT2220-Enzyme Replacement Therapy (ERT) Co-Administration Increases Pompe Enzyme (rhGAA) Activity in First 3 Dose Cohorts in Phase 2 Study**

CRANBURY, N.J., and PERTH, Australia, Oct. 11, 2012 (GLOBE NEWSWIRE) -- Amicus Therapeutics (Nasdaq:FOLD) today announced additional positive preliminary results from an ongoing Phase 2 open-label drug-drug interaction study (Study 010) to evaluate the safety and plasma pharmacokinetic (PK) effects of the pharmacological chaperone AT2220 (duvoglustat HCl) co-administered with enzyme replacement therapy (ERT) for Pompe disease (Myozyme® and Lumizyme®). These Phase 2 results were presented in a poster at the 17th International World Muscle Society Congress in Perth, Australia. The Company also announced initial findings from ex vivo studies to characterize the immunogenicity of Myozyme and Lumizyme with and without AT2220.

For people with Pompe disease, deficient GAA enzyme leads to the accumulation of glycogen in tissues affected by disease (primarily muscle). Myozyme and Lumizyme (alglucosidase alfa, or recombinant human GAA enzyme, rhGAA) are the first and only approved treatments for Pompe disease. The clinical benefit of Myozyme and Lumizyme may be limited by low stability of the recombinant enzyme at neutral pH and body temperature, modest tissue uptake, and immune responses that affect tolerability and efficacy. Published preclinical data suggest that AT2220 in combination with this ERT may improve rhGAA enzyme activity, reduce glycogen accumulation, and potentially mitigate ERT-related immunogenicity in patients with Pompe disease.

Pol F. Boudes, MD, Chief Medical Officer of Amicus Therapeutics said, "We continue to be encouraged by preliminary results from Study 010. Following co-administration, we have seen consistent increases in the amount of active enzyme in plasma in all patients, with the greatest increase in Cohort 3. We look forward to completing Study 010 in the fourth and highest dose cohort, and expect to report results by the end of the year."

**Study 010 Preliminary Results — 3 Cohorts of AT2220 Co-Administered with ERT (n=16)**

Study 010 is investigating single ascending oral doses of AT2220 (50 mg, 100 mg, 250 mg, and 600 mg) co-administered with Myozyme or Lumizyme in patients with Pompe disease. Each patient receives one infusion of ERT alone, and then a single dose of AT2220 just prior to the next ERT infusion. Highlights from the first three dose cohorts of AT2220 were as follows:

**Safety:** To date, single doses of AT2220 co-administered with ERT have been generally well-tolerated, with no drug-related adverse events reported. In addition, AT2220 was cleared from muscle to negligible levels by Day 7 in all three cohorts. Per the study protocol, an independent data safety monitoring board reviewed safety data from the first 3 cohorts and determined that the study should continue into the fourth and highest dose group (Cohort 4). Amicus has fully enrolled Cohort 4 and continues to anticipate results during the fourth quarter 2012.

**rhGAA Enzyme Activity in Plasma:** 24-hour plasma PK was measured at each infusion. Dose-related increases in rhGAA activity in plasma samples in 16 out of 16 patients following co-administration suggest an increase in properly folded, active rhGAA enzyme available for uptake into tissue.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>AT222 Dose with ERT</th>
<th>Mean Fold-Increase vs. ERT Alone (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=4)</td>
<td>50 mg</td>
<td>1.5 (1.2 to 1.6)</td>
</tr>
<tr>
<td>2 (n=6)</td>
<td>100 mg</td>
<td>1.7 (1.5 to 1.9)</td>
</tr>
<tr>
<td>3 (n=6)</td>
<td>250 mg</td>
<td>2.0 (1.6 to 2.6)</td>
</tr>
</tbody>
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**rhGAA Enzyme Activity in Plasma Area Under the Curve (AUC)**

**ERT + AT2220 vs. ERT Alone**
**rhGAA Enzyme Activity in Muscle**: Muscle biopsies were taken to measure rhGAA enzyme uptake into muscle tissue, with and without AT2220. In Cohort 1, all 4 patients received muscle biopsies on Day 7. In Cohorts 2 and 3, muscle biopsies were taken on Day 3 for half the patients, and on Day 7 for the other half of patients. In Cohort 1, no consistent change in rhGAA enzyme activity was observed. In Cohorts 2 and 3, the results suggest that more enzyme may be taken up into muscle tissue following AT2220 co-administration compared to ERT alone. Generally, Day 3 biopsies showed significantly greater levels of rhGAA activity, with or without AT2220, than Day 7.

### rhGAA Enzyme Activity in Muscle

<table>
<thead>
<tr>
<th>ERT + AT2220 vs. ERT Alone</th>
<th>Fold-Increase vs. ERT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort 1: ERT + AT2220 50 mg (n=4)</strong></td>
<td></td>
</tr>
<tr>
<td>Muscle Biopsy Day 7 (n=4)</td>
<td>0.7, 0.9, 1.0, 1.4</td>
</tr>
<tr>
<td><strong>Cohort 2: ERT + AT2220 100 mg (n=6)</strong></td>
<td></td>
</tr>
<tr>
<td>Muscle Biopsy Day 3 (n=3)</td>
<td>0.8, 1.4, 1.6</td>
</tr>
<tr>
<td>Muscle Biopsy Day 7 (n=3)</td>
<td>1.0, 1.1, 1.6</td>
</tr>
<tr>
<td><strong>Cohort 3: ERT + AT2220 250 mg (n=6)</strong></td>
<td></td>
</tr>
<tr>
<td>Muscle Biopsy Day 3 (n=3)</td>
<td>0.8, 1.0, 1.4</td>
</tr>
<tr>
<td>Muscle Biopsy Day 7 (n=3)*</td>
<td>1.0, 1.9</td>
</tr>
</tbody>
</table>

*1 ERT sample insufficient for determining fold-increase with ERT+AT2220

**Effect of AT2220 on ex vivo ERT-Related Immunogenicity**

In parallel with Study 010, Amicus is conducting ex vivo studies supported by a grant from the Muscular Dystrophy Association to evaluate the immunogenicity of Myozyme and Lumizyme, with and without AT2220. Immune responses in the form of antibodies to rhGAA occur in a majority of Pompe patients receiving Myozyme/Lumizyme infusions and may limit treatment outcomes with ERT. By stabilizing the folded and active form of the rhGAA enzyme, AT2220 may mitigate ERT-induced immunogenicity since unfolded and aggregated proteins are generally more antigenic than properly folded proteins.

The ex vivo studies are utilizing Antitope Ltd.'s EpiScreen™ assay to measure T-cell responses in human blood samples. These studies have been completed in blood samples from healthy volunteers and will be repeated in blood samples from Pompe patients in Study 010. Results may help to determine if particular human leukocyte antigen (HLA) types are predictive of an antibody response to Myozyme and Lumizyme, and whether the addition of AT2220 can decrease immunological responses induced by Myozyme and Lumizyme.

Initial studies completed using T cells from 50 healthy donor blood samples demonstrated that the addition of AT2220 may significantly reduce the immunogenicity of Myozyme and Lumizyme. Highlights were as follows.

- Myozyme alone elicited a T-cell response in 36% of samples, which decreased to 14% in the presence of AT2220.
- Lumizyme alone elicited a T-cell response in 28% of samples, which decreased to 10% in the presence of AT2220.

David J. Lockhart, PhD, Chief Scientific Officer of Amicus Therapeutics, stated, "Myozyme and Lumizyme elicit a strong T-cell response in the ex vivo EpiScreen assay, and they are both known to elicit an antibody response in most Pompe patients treated with ERT. The addition of our small molecule chaperone AT2220 reduced the observed T-cell response to both Myozyme and Lumizyme in the EpiScreen assays. We are currently conducting additional studies using blood samples from the Pompe patients in Study 010 and expect to have results by the end of the year."

EpiScreen has been used to characterize the immunogenicity of several well-known human therapeutic proteins, including Avastin and Herceptin. The assay results have correlated well with clinical immunogenicity as measured by the antibody response in patients reported in published literature.

**Study 010 Design**

**Study 010** is a Phase 2 open-label, multi-center study to evaluate the safety and PK effects of four increasing oral doses of AT2220 (50 mg, 100 mg, 250 mg, or 600 mg) co-administered with ERT (Myozyme®/Lumizyme®) versus ERT alone in individuals with Pompe disease. The study has completed enrollment of male and female patients who have been on a stable dose and regimen of ERT for at least three months.
All patients are given a regularly scheduled ERT infusion. One hour prior to the initiation of the next ERT infusion, subjects receive a single oral dose of AT2220. Plasma rhGAA activity and protein levels are evaluated during each infusion. Each patient undergoes muscle biopsies three or seven days after each infusion to measure tissue GAA enzyme activity with and without the chaperone, as well as to measure the level of AT2220 in the muscle. More information about Study 010 can be obtained by visiting www.clinicaltrials.gov; NCT1380743 or www.pompestudy.com.

About Amicus Therapeutics

Amicus Therapeutics (Nasdaq:FOLD) is a biopharmaceutical company at the forefront of developing therapies for rare diseases. The Company is developing orally-administered, small molecule drugs called pharmacological chaperones, a novel, first-in-class approach to treating a broad range of human genetic diseases. Amicus' late-stage programs for lysosomal storage disorders include migalastat HCl monotherapy in Phase 3 for Fabry disease; migalastat HCl co-administered with enzyme replacement therapy (ERT) in Phase 2 for Pompe disease; and AT2220 co-administered with ERT in Phase 2 for Pompe disease.

About AT2220 for Pompe Disease

AT2220 is an investigational, orally-administered pharmacological chaperone owned exclusively by Amicus. The Company is currently investigating AT2220 (duvoglustat HCl) co-administered with the ERT alglucosidase alfa (Myozyme/Lumizyme) in a Phase 2 study (Study 010) in individuals with Pompe disease. In published preclinical studies, AT2220-ERT co-administration resulted in significant increases in muscle rhGAA levels and decreases in glycogen levels in a mouse model of Pompe disease. Preclinical results to date also suggest that AT2220-ERT co-administration may mitigate ERT-induced immunogenicity by stabilizing the enzyme in its properly folded and active form.

Pompe disease is a lysosomal storage disease characterized by progressive skeletal muscle weakness and respiratory insufficiency. It is caused by a deficiency in GAA activity, which leads to accumulation of glycogen in tissues affected by the disease (primarily muscle). Pompe disease affects an estimated 5,000 to 10,000 individuals worldwide and is clinically heterogeneous in the age of onset, the extent of organ involvement, and the rate of progression.


Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to clinical development of Amicus' candidate drug products and the timing and reporting of results from clinical trials evaluating Amicus' candidate drug products. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "targets," "likely," "will," "would," "should" and "could," and similar expressions or words identify forward-looking statements. Such forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. The inclusion of forward-looking statements should not be regarded as a representation by Amicus that any of its plans will be achieved. Any or all of the forward-looking statements in this press release may turn out to be wrong. They can be affected by inaccurate assumptions Amicus might make or by known or unknown risks and uncertainties. For example, with respect to statements regarding the potential goals, progress, timing and results of clinical trials, actual results may differ materially from those set forth in this release due to the risks and uncertainties inherent in the business of Amicus, including, without limitation: the potential that results of clinical or pre-clinical studies indicate that the product candidates are unsafe or ineffective; the potential that it may be difficult to enroll patients in our clinical trials; the potential that regulatory authorities may not grant or may delay approval for our product candidates; the potential that preclinical studies were not carried out in accordance with applicable laws and regulations. In addition, all forward-looking statements are subject to other risks detailed in our Annual Report on Form 10-K for the year ended December 31, 2011. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, and Amicus undertakes no obligation to revise or update this news release to reflect events or circumstances after the date hereof. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.
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