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Amicus Therapeutics and GlaxoSmithKline Announce Top Line 6-Month Primary Treatment Period Results From First Phase 3 Fabry Monotherapy Study

CRANBURY, N.J. and LONDON, Dec. 19, 2012 (GLOBE NEWSWIRE) -- Amicus Therapeutics (Nasdaq:FOLD) and GlaxoSmithKline plc (GSK) today announced the 6-month primary treatment period results from the first Phase 3 global registration study (Study 011) of investigational oral migalastat HCl monotherapy in males and females with Fabry disease who had genetic mutations identified as amenable to migalastat HCl in a cell-based assay. Study 011 randomized a total of 67 patients to receive oral migalastat HCl 150 mg or placebo on an every-other-day (QOD) dosing schedule during a 6-month, double-blind primary treatment period.

Reduction of GL-3 Substrate in Kidney Interstitial Capillaries:

Globotriaosylceramide (GL-3) is the lipid substrate that accumulates in tissues of patients with Fabry disease, most notably in the kidney. GL-3 clearance from the kidney interstitial capillaries has been used as a marker of treatment effect in Fabry disease. The pre-designated primary endpoint of Study 011 was a responder analysis evaluating the number of patients who demonstrated a 50% or greater reduction in kidney interstitial capillary GL-3 after 6 months of treatment with migalastat HCl compared to placebo. During a 6-month open label follow-up period all patients received migalastat HCl. The FDA has also indicated that it will consider the 12-month efficacy and safety data from Study 011. The paired kidney biopsies from baseline and month 6 were assessed by histological scoring using the published, quantitative Barisoni Lipid Inclusion Scoring System with Virtual Microscopy (BLISS-VM).[1] This methodology will also be utilized for the evaluation of the kidney biopsies at month 12. Amicus and GSK remain blinded to the 12-month data.

In Study 011 patients with evaluable baseline biopsies, 13/32 (41%) in the migalastat HCl treatment group demonstrated a 50% or greater reduction in kidney interstitial capillary GL-3 after 6 months of study treatment versus 9/32 (28%) in the placebo group. This difference did not achieve statistical significance (p=0.3) according to the pre-specified primary endpoint analysis.

In addition to the binary responder analysis reported above, a pre-specified secondary analysis assessing the absolute percent change in kidney interstitial capillary GL-3 from baseline to month 6 was performed. Taken alone this analysis showed a median reduction of 41% in the migalastat HCl group versus a median reduction of 6% in the placebo group (p=0.093).

To date, no drug-related serious adverse events have been observed. The most common treatment emergent adverse events occurring in 10% or more of subjects were (migalastat; placebo, respectively): headache (35%; 21%); fatigue (12%; 12%); nausea (12%; 9%); nasopharyngitis, or inflammation of the nose and throat (15%; 6%); and parasthesia, or tingling sensation of the skin (9%; 12%). The 4 dropouts in this portion of the study were deemed by the investigators to be unrelated to study medication.

The 6-month secondary endpoints in Study 011 continue to be analyzed and will be presented at the Lysosomal Disease Network WORLD Symposium (LDN WORLD), to be held February 12-15, 2013, in Orlando, Florida. Secondary endpoints include urine GL-3 and renal function (iohexol GFR, eGFR and 24-hour urine protein).

John F. Crowley, Chairman and Chief Executive Officer of Amicus, stated "Consistent with our Phase 2 experience, the 6-month results from Study 011 demonstrate notable trends in kidney interstitial capillary GL-3 reduction in favor of migalastat HCl monotherapy compared to placebo. We look forward to announcing additional 6-month results at the WORLD Symposium in February, including a presentation of important secondary and tertiary endpoints in this study. We also anticipate 12-month results from this study in the first half of 2013. Once we have the 12-month data, we intend to meet with FDA to discuss a U.S. approval pathway. We continue to believe that migalastat HCl may become an important treatment option as an oral monotherapy drug for both men and women with Fabry disease who have amenable mutations."

Marc Dunoyer, Global Head of GSK Rare Diseases added, "GSK and Amicus are committed to advancing migalastat HCl as a monotherapy in Fabry patients with amenable mutations. While these 6-month data are encouraging, there is additional work to be done. We continue to analyze the 6-month results and look forward to receiving the 12-month results from this study. In addition the results of Study 012, our second Phase 3 Fabry monotherapy study, will add to the totality of our data and give us a more complete picture of the clinical effect of migalastat HCl. This study, an 18-month comparison of migalastat to ERT, with iohexol GFR as the primary endpoint, is fully recruited and due to report in 2014."

The 6-month primary treatment period in Study 011 was completed in June 2012 in 63 out of 67 randomized patients. All 63 of these patients entered the 6-month open-label follow-up period in Study 011, to continue to receive migalastat HCl or to switch from placebo to migalastat HCl. In December 2012, a total of 59 patients completed this treatment period and received an additional kidney biopsy at month 12. In addition, 57 out of 59 patients who completed Study 011 continue to receive migalastat HCl in both ongoing open-label extension studies. The results from the 6-12 month period of study 011 are expected in the first half of 2013 and will include 12-month data in the migalastat HCl group and 6-month data in the placebo crossover group.

A second Phase 3 global registration study (Study 012) is also underway to compare open-label migalastat HCl to enzyme replacement therapy (ERT) to primarily support global registration. Study 012 (The ATTRACT, or FAB-AT1001-012 Study) is a randomized, open-label 18-month Phase 3 study investigating the safety and efficacy of oral migalastat HCl 150 mg QOD compared to standard-of-care infused therapy using ERTs (Fabrazyme® and Replagal®). This study achieved final enrollment of 60 total patients in December 2012.

Study 011 Design

Study 011 - also referred to as FACETS - is one of two ongoing Phase 3 studies of migalastat HCl monotherapy being conducted by Amicus and GlaxoSmithKline (GSK). This study was designed based on feedback from the U.S. Food and Drug Administration (FDA), and is primarily intended to support U.S. registration. Study 011 randomized 67 patients (24 males and 43 females) diagnosed with Fabry disease who had genetic mutations amenable to chaperone monotherapy in a cell-based assay. For the 6-month, double-blind primary treatment period patients were randomized to migalastat HCl 150 mg or placebo on an every-other-day (QOD) oral dosing schedule. During a 6-month open-label follow up period, patients continued treatment with migalastat HCl or switched from placebo to migalastat HCl.

The primary analysis compared the number of responders in the migalastat HCl versus placebo groups, based on a 50% or greater reduction in interstitial capillary globotriaosylceramide (GL-3) during the 6-month, double-blind treatment period. GL-3 — also referred to as peritubular capillary (PTC) inclusions — is measured in kidney biopsies. Pathologists blinded to biopsy sequence used the published, quantitative Barisoni Lipid Inclusion Scoring System with virtual microscopy (BLISS-VM) for the histological evaluation of interstitial capillary GL-3 in Study 011. BLISS is a more sensitive scoring system to measure GL-3 inclusions in PTCs compared to the semi-quantitative methodology used in previous pivotal studies of enzyme replacement therapy (ERT) for Fabry disease. Secondary endpoints for Study 011 include safety and tolerability, urine GL-3 and kidney function.

About Migalastat HCl

Amicus in collaboration with GlaxoSmithKline (GSK) is developing the investigational pharmacological chaperone migalastat HCl for the treatment of Fabry disease. Amicus has commercial rights to all Fabry products in the United States and GSK has commercial rights to all of these products in the rest of world. As a monotherapy, migalastat HCl is designed to bind to and stabilize, or "chaperone" a patient's own alpha-galactosidase A (alpha-Gal A) enzyme in those patients with genetic mutations that are amenable to this chaperone in a cell-based assay. Oral migalastat HCl monotherapy is in Phase 3 development (Study 011 and Study 012) for Fabry patients with amenable mutations. Study 011 is a placebo-controlled study intended primarily to support U.S. registration, and Study 012 is comparing open-label migalastat HCl to ERT to primarily support global registration.

For patients currently receiving ERT for Fabry disease, migalastat HCl in combination with ERT may improve ERT outcomes by keeping the infused alpha-Gal A enzyme in its properly folded and active form. Migalastat HCl co-administered with ERT is in Phase 2 (Study 013) and migalastat HCl co-formulated with JCR Pharmaceutical Co. Ltd's proprietary investigational ERT (JR-051, recombinant human alpha-Gal A enzyme) is in preclinical development. Migalastat HCl is subject to evaluation by regulatory authorities before being made available as a treatment for patients.

About Fabry Disease

Fabry disease is an inherited lysosomal storage disorder caused by deficiency of an enzyme called alpha-galactosidase A (alpha-Gal A). The role of alpha-Gal A within the body is to break down specific lipids in lysosomes, including globotriaosylceramide (GL-3, also known as Gb3). Lipids that can be degraded by the action of α-Gal are called "substrates" of the enzyme. Reduced or absent levels of alpha-Gal A activity leads to the accumulation of GL-3 in the affected tissues, including the kidneys, heart, central nervous system, and skin. This accumulation of GL-3 is believed to cause the various manifestations of Fabry disease, including pain, kidney failure, and increased risk of heart attack and stroke.

It is currently estimated that Fabry disease affects approximately 5,000 to 10,000 people worldwide. However, several literature reports suggest that Fabry disease may be significantly under diagnosed, and the prevalence of the disease may be much higher.

About Amicus Therapeutics

Amicus Therapeutics (Nasdaq:FOLD) is a biopharmaceutical company at the forefront of developing therapies for rare and orphan 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 Fabry disease; and AT2220 co-administered with ERT in Phase 2 for Pompe disease.

About GlaxoSmithKline

GlaxoSmithKline - one of the world's leading research-based pharmaceutical and healthcare companies - is committed to improving the quality of human life by enabling people to do more, feel better and live longer. For further information please visit www.gsk.com.

1. Barisoni L., *et al.*, **Archives of Pathology & Laboratory Medicine**: July 2012, Vol. 136, No. 7, pp. 816-824.

Amicus Forward-Looking Statements

This press release contains, and the accompanying conference call will contain, "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to clinical development of Amicus' candidate drug products, the timing and reporting of results from preclinical studies and 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 goals, progress, timing and outcomes of discussions with regulatory authorities and 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 and clinical studies could be delayed because we identify serious side effects or other safety issues; the potential that we will need additional funding to complete all of our studies and, our dependence on third parties in the conduct of our clinical studies. Further, the results of earlier preclinical studies and/or clinical trials may not be predictive of future results. In addition, all forward looking statements are subject to other risks detailed in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2012. 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.

GlaxoSmithKline cautionary statement regarding forward-looking statements

Under the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Factors that may affect GSK's operations are described under 'Risk Factors' in the 'Financial review & risk section' in the company's Annual Report 2011 included as exhibit 15.2 to the company's Annual Report on Form 20-F for 2011.

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