



Pompe Community Update

News from Patient Advocacy

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Pompe Phase 2 Co-administration Study: AT2220-010

Amicus Therapeutics' Pompe Program is proceeding with a Phase 2 co-administration study of AT2220, the investigational pharmacological chaperone for Pompe disease, and enzyme replacement therapy (ERT). AT2220-010 is a proof-of-concept clinical research study to determine if an oral dose of AT2220 (duvoglustat hydrochloride) before an infusion of Lumizyme or Myozyme can be co-administered safely with the ERT and whether AT2220 can impact the activity and uptake of the ERT in key tissues.

AT2220, like all of Amicus' pharmacological chaperones, is an orally administered, small molecule drug designed to increase the activity of a specific protein. Pharmacological chaperones selectively bind to and stabilize the target enzyme naturally produced by a person's cells. This leads to increased enzyme activity and potentially a decrease in the accumulated substrate in affected tissues. Preclinical work conducted by Amicus' Science team has demonstrated that pharmacological chaperones have a similar effect on recombinant enzymes, or those manufactured as enzyme replacement therapy, in rats and mice.

Co-administration of ERT and Pharmacological Chaperone Pre-clinical Data

In the case of co-administration therapy, preclinical data in mouse and rat models have shown increased stability and rhGAA (ERT) activity in key muscle tissues along with increased glycogen reduction. Preclinical data suggest that when compared to ERT alone, co-administration therapy may lead to increased cell/tissue activity, reduced dose or infusion frequency, reduced antibodies, and reduced allergic reactions. (These data were presented at the 2010 Annual Meeting of the American College of Medical Genetics and at the 6th Annual WORLD Symposium 2010.)

Preclinical work has been performed in separate experiments with each of the three different pharmacological chaperone molecules for Pompe, Fabry and Gaucher diseases and the respective ERTs, resulting in consistent findings.

Therefore, Amicus is advancing its co-administration effort into Phase 2 clinical studies in

both Pompe and Fabry disease. The Fabry co-administration study began in the spring of 2011 and continues to enroll participants.

AT2220-010 Co-administration Study Design

The Pompe AT2220-010 Study will have three purposes:

- evaluate the safety of multiple doses of AT2220 administered before an ERT infusion;
- compare rhGAA enzyme activity levels and protein levels in the blood with and without co-administration with ERT; and
- evaluate the concentration of AT2220 in skeletal muscle one week after the oral dose in combination with ERT.

There will be an estimated 16 participants in this study, each receiving only one oral dose of AT2220 before one regularly scheduled ERT infusion. Each individual's total participation in the study may last approximately three months. There will be 4 patient cohorts, each with an increasing dose of AT2220.

This is an international study that will enroll participants at a variety of sites. Males and females with Pompe disease, ages 18-65, on a stable regimen and dose of either Lumizyme or Myozyme may be eligible for participation. For more information, including more detailed inclusion criteria, please speak to your healthcare provider, visit www.clinicaltrials.gov keyword search AT2220-010, where the listing of study sites is regularly updated, or email clinicaltrials@amicustherapeutics.com.

AT2220 Monotherapy Background

Earlier in the Pompe Program, the use of AT2220 as a monotherapy for Pompe disease was explored. However, after two participants experienced serious adverse events in a Phase 2 trial in February 2009, AT2220 was put on clinical hold. These events were thoroughly studied by the company and the principal investigator. The events resolved for the patients who subsequently returned to clinical baseline status. Additional questions about the drug and its dosing were investigated, including through an innovative Phase 1 study of muscle tissue pharmacokinetics in healthy volunteers. This study measured how particular muscle tissue absorbed, metabolized and eliminated AT2220. (The results of this distinctive study were presented at the 7th Annual WORLD Symposium 2011.) After careful review of these new data, the company decided to shift its AT2220 research from monotherapy to co-

administration. After data submission and discussions with the FDA, AT2220 was released from clinical hold in March 2011, thus enabling Amicus to proceed with the Phase 2 co-administration study of AT220 and ERT.

Supporting Patient and Professional Pompe Communities

Amicus continues participating in the Pompe Community by attending and sponsoring regional patient meetings and national conferences, conducting webinars with leading advocacy organizations and presenting scientific data at professional and medical conferences. Thus far in 2011, Amicus' Pompe team, with members from Patient Advocacy, Science, Clinical Research and Medical Affairs, has participated in webinars with the International Pompe Association and the Muscular Dystrophy Association, focusing on updates in the company's Pompe program and the general Pompe community. Amicus scientists presented preclinical data about Co-administration therapy at the Society for Inherited Metabolic Diseases (SIMD) conference in California and the American College of Medical Genetics (ACMG) Conference in Washington, DC. In addition, Amicus supported and attended United Pompe Foundation's (UPF) regional patient and family meetings in Seattle, Los Angeles and Loma Linda, CA in May and July and anticipates a presence at the AMDA/IPA 2011 Pompe Patient and Scientific Conference in San Antonio and the AGSD-UK Annual Conference in Birmingham, UK, both in October 2011.

As part of the larger lysosomal storage disease community, Amicus will be attending the Society for the Study of Inborn Errors in Metabolism (SSIEM) 2011 in Switzerland in August, Latin American Society of Inborn Errors of Metabolism and Neonatal Screening (SLEIMPN) in Peru in September and the American Society for Human Genetics (ASHG) Conference in Montreal in October. Additional conferences always are considered.

If you are interested in a meeting in your area for individuals with Pompe, their family members and healthcare professionals, please contact Amicus at patientadvocacy@amicustherapeutics.com

Community Feedback: The Pompe Patient Advisory Board

Twice a year, members of Amicus' Pompe Patient Advisory Board (PAB) gather either in-person or by webinar to provide the company with important insights from the patient community and to get the latest information on the Pompe program and general company

updates. In February, the group met via webinar with representatives of several functional company areas for discussions that focused on the science and Phase 1 study leading up to the then-proposed Phase 2 Co-administration study, the protocol design for the study, and general discussion about issues and concerns of the Pompe patient and family community. Patient Advocacy also organizes Fabry and Gaucher PABs, and always likes hearing from active and informed members of the Pompe community who may be interested in serving on a future PAB. Volunteer terms are for two years. **Please contact Amicus at patientadvocacy@amicustherapeutics.com**

New Website for Pompe Clinical Study

A new website is under construction dedicated to AT2220-010, the Phase 2 co-administration clinical study. The site will provide basic information about the study, including entry criteria and updated investigational sites, and links to Pompe disease community resources. Please watch for the launch of www.pompestudy.com near the beginning of September 2011.

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