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## **STUDIES PUBLISHED IN PNAS ON THE MECHANISM OF AMICUS' EXPERIMENTAL TREATMENT FOR GAUCHER DISEASE**

**Cranbury, NJ, September 20, 2006** – Amicus Therapeutics, a biopharmaceutical company developing small molecule, orally-administered pharmacological chaperones for the treatment of a range of human genetic diseases, today announced that studies of the mechanism of action of its investigational treatment for Gaucher disease were published in the September 12 edition of the *Proceedings of the National Academy of Sciences of the United States of America (PNAS)*.

Gaucher disease results from an inherited genetic mutation, which causes a deficiency in the key enzyme acid  $\beta$ -glucosidase, also known as glucocerebrosidase (GCCase). AT2101, Amicus' lead compound for Gaucher disease, is designed to selectively bind to the GCCase enzyme and help it fold into its correct three-dimensional shape. This binding and stabilization helps increase the proper movement of the enzyme from the endoplasmic reticulum (ER) to the lysosomes, the compartments in the cell where it performs its intended biological function.

In the current study, researchers performed several experiments with AT2101 on fibroblasts from a Gaucher patient with one of the most common disease-causing mutations, designated as N370S. After discovering that N370S GCCase activity was increased in cells by as much as three-fold by AT2101 treatment for five days, researchers sought to understand in more detail the mechanisms by which AT2101 increased cellular GCCase activity. Among the key findings:

- AT2101 facilitates proper folding, prevents premature degradation, and restores efficient transport of newly-synthesized N370S GCCase to the lysosomes
- AT2101 increases the total amount of N370S GCCase in the lysosomes and also leads to improved enzyme activity and lysosomal stability



“We’ve known for some time that the pharmacological chaperone AT2101 increases the activity of the key enzyme deficient in Gaucher patients, but now we have evidence of how it actually works, which is very exciting,” said study investigator Stuart A. Kornfeld, M.D., Washington University School of Medicine, St. Louis. “There is a real need for new treatment options for Gaucher disease, and these study results are very promising.”

Amicus has filed an investigational new drug application for AT2101 for the treatment of Gaucher disease and Phase I clinical trials are underway.

### **About Gaucher Disease**

Gaucher disease is the most common lysosomal storage disorder, affecting an estimated 8,000-10,000 people worldwide. Symptoms can be severe and debilitating, including an enlarged liver and spleen, abnormally low levels of red blood cells and platelets, and skeletal disease. In rare cases, there can be significant impairment of the central nervous system.

### **About Amicus Therapeutics**

Amicus Therapeutics is a biopharmaceutical company developing novel, oral therapeutics known as pharmacological chaperones for the treatment of a range of human genetic diseases. Pharmacological chaperone technology involves the use of small molecules to restore or improve biological activity in cells by selectively binding to a misfolded protein caused by a genetic mutation. Amicus is initially targeting lysosomal storage disorders, which are severe, chronic genetic diseases with unmet medical needs. Amicus is currently conducting Phase II clinical trials for its lead compound, Amigal™, for Fabry disease, and is conducting Phase I clinical trials of AT2101 for Gaucher disease. The company plans to file an IND for AT2220 for the treatment of Pompe disease in the second half of 2006.

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