

ARCA Discovery, Inc. Announces Publication of the Genetic Basis for Enhanced Response to Bucindolol

DENVER, July 17 -- ARCA Discovery, Inc., a privately held biopharmaceutical company developing genetically-targeted therapies for heart failure and other cardiovascular diseases, today commented on the results of research findings, published July 14, 2006 in the online edition of the *Proceedings of the National Academy of Sciences* (www.pnas.org) showing that a common genetic variation may help doctors identify heart failure patients who will respond well to a new drug. ARCA believes that this drug, bucindolol, will introduce the concept of personalized medicine to cardiovascular therapy. The findings come from a prospectively-designed, genetic sub study sponsored by the NIH and Veterans Administration, as part of the Beta-blocker Evaluation of Survival Trial ("BEST") Phase III clinical study of bucindolol, a third-generation beta-blocker-vasodilator. The research findings show that bucindolol is likely to be a highly efficacious therapy for many heart failure patients and can be targeted to those patients most likely to respond favorably to therapy, a major problem with current approaches to treating heart failure.

The BEST genetic sub study was conducted by researchers at the University of Maryland School of Medicine in Baltimore, the University of Colorado at Denver and Health Sciences Center in Denver, and the Veterans Administration Cooperative Studies Program in Palo Alto, California. ARCA Discovery has exclusive, worldwide rights to bucindolol, and intends to seek FDA approval of the drug during 2007.

In the placebo-controlled study, the researchers found a 38 percent reduction in the death rate and a 36 percent reduction in hospitalizations in patients who took bucindolol and also had two copies of a genetic variant in the beta-1 adrenergic receptor called 389 arginine (Arg-389). Patients with another beta-1 receptor genetic variant, glycine (Gly-389) had no clinical endpoint response to bucindolol compared to the placebo.

"These findings suggest that bucindolol could be the first cardiovascular therapy that can be targeted genetically to those patients best-suited for the drug, an approach that has been called 'personalized medicine'," said the principal investigator of the BEST genetic sub study, Stephen B. Liggett, M.D., professor of medicine and physiology at the University of Maryland School of Medicine and director of its Cardiopulmonary Genomics Program. "This personalized therapy, based on genes, gives us an opportunity to tailor therapy in a way that has long been talked about, but which we really were never able to do before," says Dr. Liggett, who is also a founding scientist of and consultant to ARCA.

"Bucindolol is within the class of drugs known as beta-blockers, because of its ability to block receptors in the heart that are activated by norepinephrine," said Dr. Michael R. Bristow, M.D., Ph.D., a cardiologist at the University of Colorado School of Medicine and one of the study's authors, and also the Founder, President and Chief Executive Officer of ARCA. "However, bucindolol has unique properties that

distinguish it from the other drugs in this class, which may be responsible for the strong interaction that bucindolol exhibits with these genetic variations, including the ability to lower norepinephrine levels as well as to block with high affinity the beta-1 Arg-389 receptor variant. The limited genetic data available from large clinical studies on other drugs in this class suggest no similar interaction with these genetic variations. In addition, bucindolol is well-tolerated by heart failure patients, and has other clinically-demonstrated benefits such as lowering heart attack rates in chronic heart failure patients. ARCA believes that the results of the BEST genetic sub study, together with the BEST overall study and other clinical trials of bucindolol, demonstrate that bucindolol will be highly efficacious for patients with moderate to severe heart failure and specific genetic profiles, and also for patients with additional risk factors such as active ischemia and diabetes."

The BEST genetic sub study was a hypothesis-driven, prospectively-designed study initiated during the BEST Trial, and its large size of 1,040 patients distinguishes it from the limited genetic studies of other heart failure drugs. In addition to results disclosed last week, the researchers also discovered another genetic variation in the BEST genetic sub study that, when combined with the Arg-389 gene, further enhances the response of heart failure patients to bucindolol, and provides an additional genetic marker for identifying those patients who should and should not receive the drug. This information was presented at the 2005 American Heart Association annual scientific meeting.

Heart failure is a serious health problem, afflicting over five million Americans and accounting for about six percent of the total U.S. healthcare budget, according to various estimates. Currently, about 280,000 Americans die each year from the disease; less than 50 percent of patients live past five years after their initial diagnosis and less than 25 percent are alive at ten years.

About ARCA Discovery, Inc:

ARCA Discovery, Inc. is a privately held biopharmaceutical company developing genetically-targeted therapies for heart failure and other cardiovascular diseases. The Company's first product is bucindolol, a third generation beta-blocker-vasodilator for advanced heart failure and other indications, that promises to be the first genetically-targeted cardiovascular drug. Bucindolol has extensive Phase III data and a unique Phase III DNA sub study. Using this sub study, ARCA's founding scientists have confirmed two genetic polymorphisms that interact with bucindolol's unique pharmacology to modify patient response. ARCA is preparing an NDA for bucindolol and intends to seek FDA approval of bucindolol during 2007.

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