Phase III Study of Gilead's Darusentan for Resistant Hypertension Meets Primary Endpoints

April 2, 2009 5:23 PM ET

Statistically Significant Decrease in Blood Pressure in Hard-to-Treat Patient Population

FOSTER CITY, Calif.--(BUSINESS WIRE)--Apr. 2, 2009-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that DAR-311 (DORADO), a Phase III clinical trial evaluating the company's endothelin receptor antagonist (ERA) darusentan for the treatment of resistant hypertension, met its co-primary efficacy endpoints of change from baseline to week 14 in trough sitting systolic blood pressure (SBP) and trough sitting diastolic blood pressure (DBP). DORADO is one of two ongoing Phase III clinical trials evaluating the safety, efficacy and tolerability of darusentan as an add-on treatment for resistant hypertension, defined as the failure to achieve goal blood pressure while adhering to full doses of an appropriate three-drug regimen that includes a diuretic. The second study, DAR-312 (DORADO-AC), is approximately 90 percent enrolled and is expected to be completed by the end of 2009.

In the DAR-311 study, reductions in mean trough sitting SBP from baseline of 8.6 mmHg, 16.5 mmHg, 18.1 mmHg and 18.1 mmHg were observed for the placebo, darusentan 50 mg, 100 mg and 300 mg groups, respectively, after 14 weeks of treatment. Reductions in mean trough sitting DBP from baseline of 5.3 mmHg, 10.1 mmHg, 9.9 mmHg and 10.7 mmHg were observed for the placebo, darusentan 50 mg, 100 mg and 300 mg groups, respectively, after 14 weeks of treatment. These results were statistically significant for all darusentan groups ($p<0.001$).

The most common treatment-emergent adverse event was peripheral edema/fluid retention, which was reported in 17, 32, 36 and 29 percent of patients in the placebo, darusentan 50 mg, 100 mg and 300 mg groups, respectively. Most cases were mild to moderate in severity. Across all study groups, 0 percent, 1.2 percent, 4.9 percent and 5.9 percent of patients in the placebo, darusentan 50 mg, 100 mg and 300 mg groups, respectively, discontinued study drug due to edema. Decreases in hemoglobin (0.19 g/dL, 0.92 g/dL, 0.93 g/dL and 1.08 g/dL in the placebo, darusentan 50 mg, 100 mg and 300 mg, respectively) and decreases in hematocrit (0.89 percent, 2.89 percent, 2.54 percent and 2.88 percent in the placebo, darusentan 50 mg, 100 mg and 300 mg, respectively) were also observed. Liver function test results were comparable between treatment groups. Observed serum aminotransferase concentrations above three times the upper limit of the normal range were reported in three patients, one each in the placebo, 100 mg and 300 mg darusentan groups. One death (sudden cardiac death) occurred during the study; this patient was receiving placebo. Full study results highlighting efficacy and safety will be submitted for presentation at a scientific meeting later this year.

"Failure to control blood pressure elevates the risk of a number of life-threatening cardiovascular conditions such as stroke, heart attack and heart failure, suggesting an unmet need for novel antihypertensive drugs with unique mechanisms of action that can be added to existing treatment regimens in patients with resistant hypertension. In this study, more than half of the patients treated with darusentan achieved goal blood pressure, as compared to approximately one quarter of patients receiving placebo," said Norbert Bischofberger, PhD, Gilead's Executive Vice President, Research and Development and Chief Scientific Officer. "We look forward to presenting full results from this study and to completing our second Phase III study, which will further characterize darusentan's safety and efficacy profile."

Darusentan is an investigational compound and has not yet been determined safe or efficacious in humans.

About the Phase III DORADO Clinical Program

The DORADO program is designed to evaluate the safety and efficacy of darusentan for reducing SBP and DBP in resistant hypertension patients currently treated with full doses of three or more antihypertensive medications, one of which is a diuretic.

DORADO (DAR-311) is an international Phase III double-blind, placebo-controlled parallel group trial, in which 379 patients were randomized to receive once-daily doses of darusentan 50 mg (n=81), 100 mg (n=81), 300 mg (n=85) or placebo (n=132).

DORADO-AC (DAR-312) is an international Phase III double-blind, placebo- and active-controlled, parallel group trial, in which approximately 770 patients will be randomized to receive darusentan (titrated to the optimal dose of 50, 100 or 300 mg once daily), an active comparator (guanfacine 1 mg once daily) or placebo. The co-primary endpoints of the trial are the changes from baseline to week 14 in trough sitting SBP and trough sitting DBP, as measured by sphygmomanometry.

For both studies, patients who complete the 14-week assessment period are eligible to enroll in long-term safety studies (DAR-311E and DAR-312E).

About Darusentan

Darusentan is a propanoic-acid class endothelin receptor antagonist (ERA) being investigated in clinical trials as an add-on oral therapy for patients with resistant hypertension. Darusentan selectively blocks the endothelin type-A (ET_A) receptor, which if activated by endothelin-1 (ET-1), leads to vasoconstriction (narrowing of blood vessels) and cell proliferation. Elevated ET-1 blood concentrations have been reported in some patients with hypertension, including several subgroups of hypertensive patients that have been historically difficult to treat.

About Resistant Hypertension

Resistant hypertension is defined as the failure to achieve goal blood pressure in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic. According to the Seventh Joint National Committee on the Prevention, Detection, Evaluation and Treatment (JNC7), an SBP of less than 140 mmHg and a DBP of less than 90 mmHg are recommended for patients with hypertension and no other serious conditions. For patients with diabetes and chronic renal disease, target systolic and diastolic blood pressures are more stringent – a SBP goal of less than 130 mmHg and a DBP goal of less than 80 mmHg.

Hypertension affects approximately one billion people worldwide. While the exact number of patients classified as resistant is unknown, estimates suggest a prevalence of anywhere between two percent and five percent of hypertensive patients in general practice settings in the United States, with significantly higher rates in specialty referral clinics. Failure to control hypertension elevates the risk of stroke, coronary artery disease, myocardial infarction, heart failure, kidney disease and cardiovascular mortality. Currently, there is no accepted standard of care for treatment of patients with resistant hypertension.

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company’s mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North America, Europe and Australia.

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that are subject to risks, uncertainties and other factors, including risks related to Gilead’s ability to complete the DORADO-AC clinical trial in the timelines currently contemplated. In addition, safety and efficacy data from the DORADO and DORADO-AC clinical trials may not warrant further development of darusentan for the treatment of resistant hypertension and feedback from regulatory authorities or results from clinical trials might result in delays or require additional trials to be performed. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead’s Annual Report on Form 10-K for the year ended December 31, 2008, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

For more information on Gilead, please call the Gilead Public Affairs Department at

1-800-GILEAD-5 (1-800-445-3235) or visit www.gilead.com.

Source: Gilead Sciences, Inc.

Gilead Sciences, Inc.
Susan Hubbard, 650-522-5715 (Investors)
Amy Flood, 650-522-5643 (Media)