Data from a Phase I/II Study Presented at the 32nd San Antonio Breast Cancer Symposium Suggest that INCB7839 in Combination with Trastuzumab May Improve Clinical Response Rates in HER2 Positive Patients with Advanced Metastatic Disease

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WILMINGTON, Del., Dec 12, 2009 (BUSINESS WIRE) -- Incyte Corporation (Nasdaq:INCY) announced today positive results from an ongoing Phase I/II clinical trial for its selective oral sheddase inhibitor, INCB7839, involving 46 patients with HER2 positive metastatic breast cancer. The results suggest that, when compared to a historical control study of trastuzumab as monotherapy, INCB7839 in combination with trastuzumab provided improvements in time to progression and response rate in patients with HER2 positive metastatic breast cancer. These improved outcomes were achieved despite the presence of more advanced disease in the study population when compared to the historical control (Baselga et al, 2005).

The improved response rate observed in this study are thought to result from an increased response in the p95HER2 positive subpopulation (n=15). INCB7839 blocks the proteolytic cleavage of the extracellular portion of the HER2 receptor releasing the extracellular domain (ECD) and creating p95HER2, a constitutively activated membrane receptor kinase. Both elevated ECD and the presence of p95HER2 have been associated with more aggressive disease and poor clinical responses to trastuzumab based regimens. In this study, INCB7839 reduced HER2 ECD plasma levels in a dose dependent manner and the combination of INCB7839 and trastuzumab markedly improved the response rate in the p95HER2 positive subset of HER2 positive breast cancer (40% response rate) when compared to historical data (11% response rate, Scaltriti et al, 2007).

In this study, the combination of INCB7839 and trastuzumab was generally well tolerated with no EGFR kinase related toxicities (rash, diarrhea), no MMP inhibitor related toxicities (musculoskeletal), and no drug related liver enzyme elevations or bone marrow toxicities. There was also no increase in cardiomyopathy (5/46 patients experienced cardiomyopathy) and no increase in thrombotic events (5/46 patients experienced a thrombotic event) from that expected for this population. All patients received low dose warfarin and low dose aspirin daily because of prior data associating INCB7839 with an increased thrombosis risk and the high underlying rate of thrombosis in this patient population.

The 7839-202 study also demonstrated that INCB7839 significantly decreased the level of plasma ErbB ligands, another marker of poor clinical outcomes. In a separate poster researchers at Incyte showed that the ErbB ligands can circumvent the anti-tumor activity of trastuzumab and lapatinib for HER2+ breast cancer cell lines. ErbB ligand-induced resistance appeared to be mediated by signaling through p95HER2 and, by inhibiting sheddase activity, INCB7839 restored the anti-tumor activity of trastuzumab and lapatinib in the presence of ErbB ligands.

A copy of the posters can be accessed by using the following links:

Clinical: 7839-202 Study - Poster 5056
Pre Clinical: 7839-202 Study - Poster 3138

Howard (Skip) Burris III, M.D., Chief Medical Officer and Director of Drug Development, Sarah Cannon Research Institute (SCRI), Nashville, Tennessee, stated, "The results of this proof of concept study, while limited to a small number of patients, are encouraging and suggest that the combination of the sheddase inhibitor with trastuzumab may offer a new therapeutic approach in HER2 positive breast cancer. The correlation of clinical activity with markers demonstrating inhibition of HER2 cleavage supports the role that INCB7839 may have in improving clinical outcomes, particularly in the 25 to 30% of HER2 over-expressing breast cancers that express p95HER2. We look forward to INCB7839 progressing into controlled studies that add INCB7839 to established trastuzumab containing regimens."

Richard Levy, M.D., Incyte's Executive Vice President, Chief Drug Development and Medical Officer, stated, "If these results are confirmed with additional data from the ongoing clinical trial, I believe there may be a clear path to registration by studying the p95HER2 positive subset of patients. Importantly, the data suggest that comparative clinical trials of modest size would be sufficient to demonstrate improvements in progression free survival in this population of patients that have a poor response to the current HER2 directed regimens."

About Study 7839-202

The purpose of this Phase I/II, modified dose escalation, open label trial was to determine the therapeutic effect and safety of INCB7839 combined with trastuzumab in patients with previously untreated HER2 positive metastatic breast cancer. The study consisted of a dose escalation phase followed by an expansion phase at a dose of 300 mg BID. The study is ongoing and now allows the addition of chemotherapy to the INCB7839 + trastuzumab combination.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based drug discovery and development company focused on developing proprietary small molecule drugs for oncology, inflammation and diabetes. Incyte's most advanced compound, INCB18424, is in Phase III development for myelofibrosis. For additional information on Incyte, visit the Company's web site at www.incyte.com.

Forward-Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements with respect to the possibility of the sheddase inhibitor INCB7839 with trastuzumab offering a new therapeutic approach in HER2 positive breast cancer, INCB7839 progressing into controlled studies, the possibility of a clear path to registration by studying the p95HER2 positive subset of patients and comparative clinical trials of modest size being sufficient to demonstrate improvements in progression free survival in the population of patients that have a poor response to the current HER2 directed regimens, are all forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities

Litigation Reform Act of 1995. These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially, including the high degree of risk associated with drug development and clinical trials, the uncertainty of the FDA approval process, results of further research and development, the impact of competition and of technological advances and the ability of Incyte to compete against parties with greater financial or other resources, Incyte's ability to enroll a sufficient number of patients for its clinical trials, and other risks detailed from time to time in Incyte's filings with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2009. Incyte disclaims any intent or obligation to update these forward-looking statements.

SOURCE: Incyte Corporation

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