

## New Preliminary Data from Two Studies Show Clinical Activity of Neratinib in Combination with Trastu

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Wyeth Pharmaceuticals, a division of Wyeth announced preliminary data from two ongoing studies, one evaluating neratinib in combination with trastuzumab in HER-2 positive breast cancer, and a separate study investigating neratinib safety and efficacy when given with paclitaxel (Taxol®, Bristol-Myers Squibb) in patients with HER-2 dependent solid tumors. The data gathered from both trials are scheduled to be presented at the 45th Annual Meeting of the American Society of Clinical Oncology Annual Meeting in Orlando, Florida, from May 29 to June 2, 2009. Neratinib is an investigational orally administered irreversible inhibitor of the HER-2 and EGFR kinases.

Ramona Swaby, M.D., Department of Medical Oncology, Fox Chase Cancer Center, Philadelphia, PA said, The data gathered from these studies provide additional evidence suggesting that neratinib, when combined with these therapies, is an active agent in HER-2 positive breast cancer. While improvements have been made in treating HER-2 positive breast cancer, there remains an unmet medical need for more therapies for patients with metastatic breast cancer. These data warrant ongoing and future investigations to further understand and evaluate the utility of neratinib against this aggressive disease. Neratinib (HKI-272) in Combination with Trastuzumab for the Treatment of Advanced Breast Cancer This ongoing phase 1/2 study of neratinib in combination with trastuzumab evaluated patients with advanced ErbB-2 positive breast cancer that progressed following therapy with trastuzumab, the standard of care in this disease setting. The primary endpoint of the two-part study is 16-week progression-free survival (PFS). The first part of the study includes patients being administered neratinib (160 mg or 240 mg) daily plus weekly trastuzumab (4 mg/kg IV loading dose then 2 mg/kg). In the second part of the study, patients receive a weekly dose of trastuzumab with daily neratinib (240 mg). To date, 45 patients have been enrolled and 28 patients were evaluable for efficacy. The 16-week PFS rate (for part 2) was 45 percent (95 percent CI, 26 percent to 62 percent); median PFS was 16 weeks (95 percent CI, 15 to 31 weeks). The complete response rate was 7 percent, while 21 percent of evaluable patients showed partial response. The objective response rate was 29 percent (95 percent CI, 13 percent to 49 percent). In this study, adverse events of any grade were diarrhea, nausea, anorexia, vomiting, asthenia, rash and fatigue. In the 45 patients enrolled in this study, diarrhea was the most common adverse event, observed in 91 percent of patients, and was the most significant grade 3 or 4 adverse event, occurring in 16 percent of patients. Two patients receiving neratinib 240 mg reported adverse events leading to discontinuation of therapy.

Safety and Efficacy of Neratinib (HKI-272) in Combination with Paclitaxel in Patients with Solid Tumors In a separate phase 1/2, open-label, 2-part study, ascending multiple daily oral doses of neratinib (160 mg, 240 mg) were administered in combination with IV paclitaxel 80 mg/m<sup>2</sup>, if tolerable, or 70 mg/m<sup>2</sup> on days 1, 8 and 15. Patients with solid tumors (endometrial, cervical, colorectal and esophageal cancers) were entered in the phase 1 portion (part 1), and only patients with metastatic ErbB-2 positive breast cancer were enrolled in part 2. Safety and efficacy were investigated in patients with ErbB-2 positive metastatic breast cancer. A total of 102 patients were enrolled in part 2 of the study and 97 patients were evaluable for efficacy. The overall response rate at 16-weeks (for part 2) was 63 percent (80 percent CI, 55.9 percent to 69.4). In this preliminary analysis, the adverse event profile of the combination of neratinib (240 mg) plus paclitaxel (80 mg/m<sup>2</sup>) was similar to that reported with both agents as monotherapy. Adverse events of any grade were diarrhea, alopecia, infection, peripheral neuropathy, leucopenia, anemia, nausea, rash, fatigue and vomiting. The most common adverse event was diarrhea, observed in 89 percent of the 102 patients enrolled in part 2 and was the most significant grade 3 or 4 adverse event, occurring in 25 percent of patients. Fourteen patients had dose reductions and one patient withdrew from the study due to an adverse event. Emerging clinical data continue to suggest that neratinib, in combination with these therapies is tolerable and active in treating HER-2 positive disease, even in those women who have progressed while on other targeted therapies," says Gary L. Stiles, M.D., Chief Medical Officer, Wyeth Pharmaceuticals. "These additional data build upon results presented at the 2008 San Antonio Breast Cancer Symposium, and Wyeth is committed to evaluating further the potential of this investigational therapy. In 2008, the American Cancer Society estimated that more than 182,000 women in the United States would be diagnosed with breast cancer, and more than 40,000 would die from the disease. The HER-2 receptor is over-expressed in 25 percent to 30 percent of patients with breast cancer. About Wyeth Wyeth is one of the world's largest research-driven pharmaceutical and health care products companies. It is a leader in the discovery, development, manufacturing and marketing of pharmaceuticals, vaccines, biotechnology products, nutritionals and non-prescription medicines that improve the quality of life for people worldwide. The Company's major divisions include Wyeth Pharmaceuticals, Wyeth Consumer Healthcare and Fort Dodge Animal Health.