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Pfizer Data Identify Certain Lung Cancer Patients Who May Benefit from Treatment with Figitumumab

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Research explores biomarkers as potential predictors of sensitivity to treatment

(BUSINESS WIRE)--Pfizer announced today results from studies evaluating the company's investigational anti-insulin growth factor- type 1 receptor (IGF-1R) antibody, figitumumab (CP-751,871), in patients with non-small cell lung cancer (NSCLC). A total of three abstracts were presented at the 45th Annual American Society of Clinical Oncology (ASCO) annual meeting in Orlando.

"As we try to find the right drug to use in the right setting for each patient, we are encouraged by these data, suggesting a relationship between tumor histology and response to figitumumab," said Dr. Mace Rothenberg, senior vice president of clinical development and medical affairs for Pfizer's Oncology Business Unit. "Given that patients with advanced NSCLC face a poor prognosis, it is important to be able to identify specific patients who may benefit most from different treatment options."

Lung cancer is the most common cancer worldwide. NSCLC accounts for about 85 percent of lung cancer cases and remains difficult to treat, particularly in the metastatic setting. Nearly 60 percent of NSCLC patients are diagnosed late with Stage IIIB/IV advanced disease. In Stage IV patients, the five-year survival rate is only two percent. For all stages of NSCLC, the five-year survival rate is only 15 percent.

Over 60 Percent Response Rate Observed in 56 Patients with Squamous Cell Carcinoma NSCLC Treated with Chemotherapy Plus Figitumumab

A single-arm extension cohort (n=56) was conducted to confirm the preliminary findings from a randomized Phase 2 study of 156 patients, which evaluated overall response with figitumumab in combination with carboplatin and paclitaxel in patients with NSCLC. The Phase 2 study suggested a dose-response relationship in patients with squamous cell carcinoma and adenocarcinoma.

In the extension cohort study, 56 patients with non-adenocarcinoma NSCLC (squamous cell, large cell, and not otherwise specified) were enrolled and treated with figitumumab (20 mg/kg), plus carboplatin (AUC of 6) and paclitaxel (200 mg/m2). As measured by RECIST (Response Evaluation Criteria in Solid Tumors), 27 out of 42 squamous cell patients (64.3 percent) demonstrated a response. One complete and 26 partial responses were observed. In fifteen of the 26 partial responses, there was a 50 to 95 percent reduction in tumor size. Of 10 patients with large cell carcinoma/not otherwise specified tumors, two partial responses were seen.

"Despite improvements in treatment, NSCLC is a heterogeneous disease that remains difficult to control," said Dr. Daniel Karp, director of The University of Texas M. D. Anderson Cancer Center Clinical and Translational Research Center (CTRC). "The striking reductions in tumor size seen in squamous NSCLC patients treated with figitumumab in combination with carboplatin and paclitaxel are encouraging for this patient population with

limited treatment options."

Twenty patients received single-agent figitumumab upon discontinuation of chemotherapy. Reductions in tumor size with figitumumab maintenance treatment were observed in two patients. Median progression-free survival (PFS) was 5.7 months for the overall extension cohort (n=56), 5.9 months for patients with squamous cell carcinoma (n=46) and 3 months for patients with large cell carcinoma and not otherwise specified tumors (n=10).

Figitumumab was generally well-tolerated in the extension cohort. The most common grade 3/4 adverse events were hyperglycemia (11 percent), fatigue (7 percent), and neutropenia (5 percent). Hyperglycemia almost always occurred within the first treatment cycle and was generally manageable with standard measures.

Free IGF-1 as a Plasma Biomarker That May Predict Response to Figitumumab

Results from translational research conducted as part of the randomized Phase 2 study of figitumumab in combination with carboplatin and paclitaxel in NSCLC patients suggest that the amount of biologically active free IGF-1 (fIGF-1) in plasma may help predict which patients will respond to figitumumab therapy. A total of 156 patients were enrolled in the Phase 2 portion of the study. Baseline blood samples were obtained from 116 patients.

High fIGF-1 appeared to be a marker for resistance to chemotherapy, with median PFS as low as 2.1 months for patients in the highest fIGF-1 quartile (P=0.11). Patients with elevated baseline fIGF-1 levels appeared particularly sensitive to figitumumab. Study findings showed that adding figitumumab (20 mg/kg) to chemotherapy in patients with high levels of fIGF-1 increased PFS, versus treatment with paclitaxel and carboplatin alone (by 3.4 months, 6 months vs. 2.6 months, respectively, P=0.001 for patients with fIGF-1 >0.6 ng/mL, and by 3.9 months, 6 months vs. 2.1 months, respectively, p=0.001, for patients with fIGF-1 >0.9 ng/mL).

In summary, results from this study suggest that determining baseline levels of free IGF-1 may contribute to the identification of patients who may respond to treatment with figitumumab.

Exploring Additional Biomarkers As Predictors of Sensitivity To Figitumumab In NSCLC

Data presented at ASCO reports on IGF-1R pathway and epithelial-mesenchymal transition (EMT) biomarkers that may inform the design of future trials of figitumumab in advanced NSCLC.

In this study, authors analyzed 151 blood samples from 42 patients enrolled in the randomized Phase 2 study of figitumumab in combination with carboplatin and paclitaxel in NSCLC patients. They observed elevated plasma levels of fIGF-1 in patients with adenocarcinoma compared with those with squamous cell carcinoma (P=0.0326) and with large cell carcinoma (P=0.026).

In patients with squamous cell carcinoma, expression of fIGF-1 was greatest in patients with objective partial responses, compared with those with stable disease or progressive disease (P=0.02).

A PFS advantage was observed with the addition of figitumumab to the chemotherapy regimen of adenocarcinoma patients with fIGF-1 levels in the highest quartile. In patients with adenocarcinoma, those receiving the highest figitumumab dose (20 mg/kg) in combination with paclitaxel and carboplatin and in the highest quartile of fIGF-1, experienced the longest median PFS (P=0.0039).

In summary, these results suggest that IGF-1R overexpression and increased free IGF-1 may be key independent mechanisms of sensitivity to figitumumab in NSCLC. These findings warrant further investigation.

Figitumumab Phase 3 Clinical Trial Program

Pfizer recently initiated a large global Phase 3 clinical trial program, ADVIGO (ADVancing IGF-1R in Oncology), to further evaluate figitumumab in NSCLC.

- ADVIGO 1016 (Currently Enrolling): Randomized, Open-Label, Phase 3 Trial Of Figitumumab (CP-751,871) in Combination with Paclitaxel and Carboplatin Versus Paclitaxel and Carboplatin in Patients with Non-Small Cell Lung Cancer
- ADVIGO 1017 (Enrolling Soon): Randomized, Open-Label, Phase 3 Trial To Evaluate The Effect of the Addition of Figitumumab (CP-751,871) to Gemcitabine and Cisplatin in Patients with Advanced NSCLC
- ADVIGO 1018 (Currently Enrolling): Randomized, Open-Label, Phase 3 Trial of Erlotinib Alone or in Combination with Figitumumab (CP-751,871) in Patients with Advanced NSCLC of Non-Adenocarcinoma Histology

Pfizer is committed to the development of figitumumab and has invested significant resources in the Phase 3 program, which will include more than 2,500 patients around the world.

- For more information on the ADVIGO 1016 and 1018 trials, please visit, www.clinicaltrials.gov.

About Figitumumab (CP-751,871)

Figitumumab, an investigational fully human monoclonal antibody, is a highly specific inhibitor of the insulin growth factor-1 receptor (IGF-1R) pathway. The IGF-1R pathway is thought to be one of the fundamental signaling pathways that leads to uncontrolled growth and survival of tumor cells, and may represent a resistance mechanism against EGFR inhibitors and other anti-cancer therapies.

In addition to NSCLC, Pfizer is studying figitumumab in clinical trials for the potential treatment of other cancers, including prostate, breast and colon cancers, and Ewing's sarcoma. To date, more than 1,000 patients have participated in figitumumab clinical trials in multiple tumor types.

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options for cancer patients worldwide. Our robust pipeline consists of 21 biologics and small molecules in clinical development across four scientific platforms – anti-angiogenesis, signal transduction, immuno-oncology, and cytotoxic potentiators. Pfizer Oncology has over 200 clinical trials including robust Phase 3 clinical trial programs in renal cell carcinoma, prostate cancer, non-small cell lung cancer, metastatic breast cancer, colorectal cancer, and hepatocellular carcinoma.

By working collaboratively with academic institutions, researchers, governments and licensing partners, Pfizer Oncology strives to transform treatment by targeting the right drug for the right patient at the right time.

For more information please visit www.Pfizer.com.

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DISCLOSURE NOTICE: The information contained in this release is as of May 30, 2009. Pfizer assumes no obligation to update any forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information that involves substantial risks and uncertainties about biomarkers that may predict responsiveness to figitumumab (CP-751,871) in patients with non-small cell lung cancer; about various potential indications, including non-small cell lung cancer, for figitumumab; and about the potential benefits of figitumumab. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by regulatory authorities regarding whether and when to approve any drug applications that may be filed for any such indications as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of any such indications; and competitive developments.

A further list and description of risks and uncertainties can be found in Pfizer’s Annual Report on Form 10-K for the fiscal year ended December 31, 2008 and in its reports on Form 10-Q and Form 8-K.

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