A7471017 – Dacomitinib (PF-00299804) Phase 2 Trial
First-line dacomitinib, an irreversible pan-HER tyrosine kinase inhibitor for patients with EGFR-mutant lung cancers (Abstract #7530)

Data Fact Sheet

Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2012

Dacomitinib is an investigational agent and has not been approved for marketing by any regulatory agency at this time.

| Trial Design | • This study is a global, multicenter, open-label Phase 2 study evaluating dacomitinib as a first-line treatment in patients with non-small cell lung cancer (NSCLC), enriched for an EGFR activating mutation or patients with HER2 amplification or mutation.1, 2
| | • 106 patients are expected to be enrolled in this study and receive treatment with oral dacomitinib 45 mg, or 30 mg with escalation to 45 mg, with assessments occurring every 28 days.1, 2

| Endpoints | Primary Endpoint 1, 2
| | • Progression-free survival (PFS) rate at four months

| | Key Secondary Endpoints 1, 2
| | • Best overall response according to RECIST
| | • Duration of response (DR)
| | • Overall survival (OS)
| | • PFS
| | • Evaluation of the overall safety profile, based on physical examination, laboratory tests, and adverse events (AEs)
| | • Patient Reported Outcomes (PRO) of health-related quality of life (HRQOL) and improvement in lung cancer symptoms
| | • Evaluation of trough concentrations of PF-00299804 after repeated dosing

| | Exploratory endpoints also include:
| | • EGFR and HER signaling pathways in blood and tissue at baseline and on study
| | • PFS in patients with HER2 amplification or mutation

| Eligibility Criteria for EGFR Mutated NSCLC Cohort | Key Inclusion Criteria 1, 2
| | • 18 years or older
| | • Histologically confirmed advanced NSCLC of adenocarcinoma subtype or mixed adenosquamous histology
| | • Light- or non-smokers or known EGFR activating mutation
| | • Eastern Cooperative Oncology Group (ECOG) performance status 0 – 1

| | Key Exclusion Criteria 1, 2
| | • Active brain metastases
| | • Prior systemic therapy for advanced disease
| | • Known EGFR wild-type NSCLC
## Patient Characteristics

- EGFR mutational status was determined in 53 patients, including 46 patients (87 percent) with EGFR mutated exons 19 and 21 and seven patients (13 percent) with other EGFR mutations.\(^1,2\)
- 32 of the 46 patients with EGFR mutated exons 19 and 21 were female (70 percent), 26 (57 percent) were Asian and 37 (80 percent) were never smokers.\(^1,2\)
- In patients with other EGFR mutated exons, four (57 percent) were female, two (29 percent) were Asian and four (57 percent) were never smokers.

## Results Presented at ASCO 2012

- The data presented at ASCO is from the EGFR cohort of this study. The HER2 cohort is currently recruiting patients and data is not yet available.
- The trial demonstrated that 96 percent (95 percent CI: 84 – 99) of patients in the study with EGFR exon 19 or 21 mutations were progression free at four months, the primary endpoint of the study, and preliminary median progression free survival for these patients was 17 months (95 percent CI: 13 – 24).
  - 74 percent (95 percent CI: 58 – 85) of patients remained progression free at one year.\(^1\)
  - 74 percent of patients in this cohort experienced a partial response (95 percent CI: 59 – 86).\(^1\)
  - There were 21 Grade 3 adverse events and two Grade 4 adverse events. There were no treatment-related deaths.
  - The most common side effects included diarrhea and skin and nail changes.
  - Three out of 46 patients in the cohort of patients with EGFR exon 19 or 21 mutations discontinued dacomitinib due to treatment-related side effects.\(^1\)

## Conclusions

- Dacomitinib shows encouraging efficacy as a first-line treatment in patients with non-small cell lung cancer (NSCLC) enriched for an EGFR activating mutation based on clinical selection factors, or confirmation of molecular status.\(^1\)

## Ongoing Trials with Dacomitinib

- Clinical evaluation of dacomitinib is ongoing in a number of clinical trials in patients with advanced NSCLC across lines of therapies and a range of histologies and molecular subtypes, such as EGFR and KRAS status. Currently, there are two Phase 3 studies ongoing for dacomitinib.
  - ARCHER 1009 is a randomized, double-blind, multicenter trial evaluating dacomitinib versus erlotinib for the second/third-line treatment of patients with locally advanced or metastatic NSCLC following progression after, or intolerance to, at least one prior chemotherapy. This trial is open for enrollment and the study design will be presented at ASCO (Abstract #TPS7615).\(^3\)
  - BR.26 is a double-blind, placebo-controlled randomized trial evaluating dacomitinib in patients with advanced NSCLC with varying histologies and molecular subtypes, after failure of at least one chemotherapy regimen and erlotinib or gefitinib (NCIC-Clinical Trial Group led trial).\(^4\)

## Investigators

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1 ASCO Poster Discussion #7530. First-line dacomitinib (PF-00299804), an irreversible pan-HER tyrosine kinase inhibitor, for patients with EGFR-mutant lung cancers. Tuesday, June 5. 8:00 AM. Dr. Mark G. Kris. American Society of Clinical Oncology (ASCO) Annual Meeting 2012. Chicago. June 1 – 5, 2012.

