Crizotinib (PF-02341066) is an investigational agent and has not been approved by regulatory agencies.

**ABOUT CRIZOTINIB (PF-02341066)**
- Crizotinib (PF-02341066) is a first-in-class compound that inhibits the anaplastic lymphoma kinase, or ALK, and is representative of Pfizer’s personalized medicine approach to cancer treatment.¹
- Crizotinib (PF-02341066) is also an inhibitor of c-MET, a mesenchymal-epithelial transition factor.
  - The role of crizotinib’s c-MET activity is under investigation.²
- By inhibiting ALK, crizotinib (PF-02341066) blocks signaling in a number of cell pathways that may be critical for the growth and survival of tumor cells.³

**ALK AND CANCER**
- Scientific advances have led to the identification of ALK as a new therapeutic target in cancer.⁴
- Originally discovered in anaplastic large cell lymphomas, alterations in the ALK gene have since been identified as an important factor in cancers such as non-small-cell lung cancer (NSCLC), anaplastic large cell lymphomas (ALCL), inflammatory myofibroblastic tumors (IMT), neuroblastomas and rare sarcomas.²
  - Preliminary epidemiology suggests that approximately 3-5 percent of NSCLC tumors are ALK-positive.² In NSCLC, this alteration leads to activation of the ALK fusion gene, believed to be a tumor-exclusive target that is a key driver of oncogenesis, or tumor development.²
  - An estimated 70-80 percent of ALK-positive ALCL carry the nucleophosmin (NPM)-ALK fusion protein.²
    - The majority of pediatric ALCL cases (80-90 percent) are ALK-positive.
  - Rearrangements involving the ALK receptor kinase have been detected in over 50 percent of IMTs.⁵
  - Activating mutations in the tyrosine kinase domain of the ALK oncogene account for the majority of cases of hereditary neuroblastoma.⁶
- When ALK is inhibited, important growth and survival pathways in tumor cells are blocked, which may lead to stabilization or regression of tumors.²
- Molecular testing upon diagnosis may help to identify the appropriate treatment strategy for patients with a variety of advanced cancers.
  - For example, patients with advanced NSCLC may be evaluated for ALK status by molecular characterization of the tumor, through either a previously surgically-removed pathology specimen, or from a core biopsy.³

**CLINICAL STUDIES**
Pfizer is continuing to explore a clinical development program to determine whether patients may benefit from crizotinib (PF-02341066). Following is a list of some of the crizotinib trials that are currently ongoing:

**Phase 3**
- PROFILE 1007 (A8081007) – Randomized, open-label study of efficacy and safety of crizotinib (PF-02341066) versus standard of care chemotherapy in advanced NSCLC patients with an alteration in the ALK gene, who have failed one prior treatment with a platinum-based chemotherapy.⁷

**Phase 2**
- PROFILE 1005 (A8081005) – Open-label, single-arm study of efficacy and safety of crizotinib (PF-02341066) in NSCLC patients with an alteration in the ALK gene, who have failed more than one line of treatment with prior chemotherapy.⁸
**Phase 1**
- **PROFILE 1001 (A8081001)** – Phase 1 open-label, single-arm, dose-escalation study with an expansion cohort evaluating the safety, pharmacokinetic and pharmacodynamic of crizotinib (PF-02341066), administered orally to patients with advanced cancer.

**Phase 1/2**
- **PROFILE 912 (ADVL0912)** – Ongoing study of crizotinib (PF-02341066) to determine the maximum dose that is safe and tolerable, and to obtain preliminary clinical activity data in pediatric patients with relapsed/refractory solid tumors, primary CNS tumors and anaplastic large cell lymphoma (ALCL). **Note: This study is being led by the Children’s Oncology Group. This is not a Pfizer-sponsored study.**

**Planned Studies**

**Phase 3 (Anticipated to Begin Early 2011)**
- **PROFILE 1014 (A8081014)** – Randomized, open-label study of the efficacy and safety of crizotinib (PF-02341066) versus standard chemotherapy in previously untreated patients with ALK-positive advanced NSCLC.

**Phase 1b (Anticipated to Begin Early 2011)**
- **PROFILE 1013 (A8081013)** – Study of safety and potential clinical activity of crizotinib (PF-02341066) in patients with diagnoses other than NSCLC whose tumors are ALK-positive. Tumor types include anaplastic large cell lymphoma (ALCL), inflammatory myofibroblastic tumor (IMT) and neuroblastoma.

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