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Pfizer Oncology To Present Broad Array Of New Pre-Clinical And Clinical Data From Early And Late Stage Compounds

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"Pfizer has exciting research underway in its early pipeline providing the preclinical rationale for potential future treatment options for cancer patients,"

(BUSINESS WIRE)--Pfizer Oncology will present nearly 30 abstracts highlighting research in new and established pathways, including inhibition of Hedgehog signaling (PF-04449913);[1] dual inhibition of PI3K/mTOR (phosphatidylinositol 3-kinase/mammalian target of rapamycin)(PF-04691502);[2] and cancer stem cell-based targets.[3] Data from this research as well as data from studies involving investigational compounds, including crizotinib,[4] an oral first-in-class compound that inhibits the anaplastic lymphoma kinase, or ALK, will be presented at the upcoming American Association for Cancer Research (AACR) 102nd Annual Meeting 2011 in Orlando, FL from April 2-6.

“Pfizer has exciting research underway in its early pipeline providing the preclinical rationale for potential future treatment options for cancer patients,” said Robert Abraham, PhD, senior vice president and chief scientific officer, Oncology Research Unit, Pfizer Worldwide Research and Development. “The data we will present at AACR are focused on the biology and basic science behind cancer and tumor growth, which may ultimately help us to improve patient outcomes.”

At AACR, Pfizer will present preclinical data from emerging fields of cancer research, including:

- *PF-04449913*

  Data evaluating the efficacy of PF-04449913, Pfizer’s small molecule, oral inhibitor of Smoothened (SMO), one of the key components of the Hedgehog signaling pathway, in inhibiting tumor growth in preclinical models (Abstract #4504, April 5).[1] Research has shown that the Hedgehog signaling pathway is essential in human development for cell regulation and maintenance at multiple levels; however, over-expression of hedgehog signaling in adults may lead to irregular activation important for tumor proliferation, survival, and/or metastasis.[5,6]

- *PF-04691502*

Preclinical data evaluating PF-04691502, an orally administered, dual PI3K/mTOR inhibitor as a single agent and in combination with another Pfizer investigational compound, PD-0325901, a mitogen-activated extracellular signal regulated kinase kinase (MEK) inhibitor (Abstract #4480, April 5).[2] The PI3K signaling pathway plays a critical role in regulating basic cellular functions including growth, metabolism and survival,[7] and is a frequently dysregulated pathway in human cancer.[8] The mammalian target of rapamycin (mTOR) is a downstream mediator in the PI3K pathway.[9] Pfizer is also developing an intravenously administered dual PI3K/mTOR inhibitor, PF-05212384 (also known as PKI-587).

- *Cancer stem cell research*

  New research exploring the oncofetal protein 5T4, expressed on cancer stem cells (CSCs), or tumor-initiating cells (TICs), as a potential new therapeutic target (Abstract #475, April 3).[3] 5T4 is a tumor-associated protein which has been linked with advanced disease and poor clinical outcome in a number of cancers.[10,11]

Pfizer will also present clinical data highlighting compounds from the company's oncology pipeline:

- *Crizotinib*

  Research summarizing pre-clinical pharmacology studies for crizotinib in anaplastic lymphoma kinase (ALK)-positive tumor models, including the evaluation of antitumor efficacy of crizotinib in ALK-positive non-small cell lung cancer (NSCLC) tumors (Abstract #LB-390, April 5) will be presented.[4] Additional research being presented focuses on how crizotinib works, identification of mechanisms of resistance,[12] its potential role in treating neuroblastoma[13] and its effects on vision.[14]

- *Sunitinib*

  Correlations between germline genotype and safety/efficacy endpoints in a clinical trial of sunitinib in patients with metastatic colorectal cancer (mCRC)(Abstract #289, April 3).[15]

- *PF-00299804*

  Results from a Phase 1 open-label single-radiolabeled dose study of PF-00299804 (PF-299) in healthy male volunteers (Abstract #1291, April 4).[16]

Pfizer & Stand Up to Cancer

Pfizer is proud to be a Stand Up to Cancer (SU2C) donor. SU2C is a cutting edge initiative created to accelerate groundbreaking cancer research, for which AACR is the scientific partner.[17]

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide. Our strong pipeline, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. Pfizer Oncology has biologics and small molecules in clinical development and more than 100 clinical trials underway. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments, and licensing partners, Pfizer Oncology strives to cure or control cancer with breakthrough medicines, to deliver the right drug for each patient at the right time. For more information please visit www.Pfizer.com.

DISCLOSURE NOTICE: The information contained in this release is as of April 1, 2011. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about various oncology product candidates and potential additional indications for various in-line oncology products, including their potential benefits, that involves substantial risks and uncertainties. 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 or supplemental drug applications that have been or may be filed for any such oncology product candidates or any such additional indications for in-line oncology products as well as their decisions regarding labeling and other matters that could affect their availability or commercial potential; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2010 and in its reports on Form 10-Q and Form 8-K.

[1] AACR Accepted Abstract #4504. PF-04449913, a small molecule inhibitor of Hedgehog signaling, is effective in inhibiting tumor growth in preclinical models. Poster session, Tuesday, April 5, 2011: 1:00-5:00 PM. A. Jackson-Fisher – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.

[2] AACR Accepted Abstract #4480. Combination of a PI3K/mTOR inhibitor and a MEK inhibitor at suboptimal dose significantly inhibits growth of lung adenocarcinoma tumors in KrasG12D-LSL mice Poster session, Tuesday, April 5, 2011: 1:00 -5:00 PM. F. Shojaei – Presenter. American Association for Cancer Research 102 nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.

[3] AACR Accepted Abstract #475. Delineation of a cellular hierarchy in lung cancer reveals an oncofetal antigen expressed on tumor-initiating cells. Poster session, Sunday, April 3, 2011: 1:00-5:00 PM. M. Damelin – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.

[4] AACR Accepted Abstract #LB-390. Antitumor efficacy of crizotinib (PF-02341066), a potent and selective ALK and c-MET RTK inhibitor, in EML4-ALK driven NSCLC tumors in vitro and in vivo. Poster session, Tuesday, April 5, 2011: 1:00 -5:00 PM. H. Zou – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.

[5] Jiang J and Hui C. Hedgehog Signaling in Development and Cancer. Developmental Cell. 2008; 15:801-812.

[6] Low JA and de Sauvage FJ. Clinical Experience With Hedgehog Pathway Inhibitors. J Clin Oncol. 2010; 28:5321-5326.

[7] Serra V et al. NVP-BEZ235, a Dual PI3K/mTOR Inhibitor, Prevents PI3K Signaling and Inhibits the Growth of Cancer Cells with Activating PI3K Mutations. Cancer Research. 2008; 68: 8002-8030.

[8] Hennessy B et al. Exploiting the PI3K/mTOR Pathway for Cancer Drug Discovery. Nature. 2005; 4: 988-1004.
[9] Gridelli C et al. The Potential Role of mTOR Inhibitors in Non-Small Cell Lung Cancer. The Oncologist. 2008;13:139-147.
[10] Boghaert ER, Sridhara L, Khandke KM et al. The oncofetal protein, 5T4, is a suitable target for antibody-guided anti-cancer chemotherapy with calicheamicin. Int J Oncol. 2008; 32: 221-234,
[11] Ward CM, Barrow K, Woods AM et al. The 5T4 oncofoetal antigen is an early differentiation marker of mouse ES cells and its absence is a useful means to assess pluripotency. J Cell Science. 2003; 116, 4533-4542.
[12] AACR Accepted Abstract #742. Mechanisms of resistance to small molecule inhibition of anaplastic lymphoma kinase in human neuroblastoma. Poster session, Sunday, April 3, 2011: 1:00 -5:00 PM. E. Carpenter – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.
[13] AACR Accepted Abstract #4563. Antibody targeting of anaplastic lymphoma kinase induces cytotoxicity of human neuroblastoma. Poster session, Tuesday, April 5, 2011: 1:00 -5:00 PM. E. Carpenter – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.
[14] AACR Accepted Abstract #4385. Effect on retinal function as a mechanism for vision disorders with crizotinib (PF-02341066). Poster session, Tuesday, April 5, 2011: 1:00 -5:00 PM. D. Matsumoto – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.
[15] AACR Accepted Abstract #289. Associations between germline genotype and efficacy and safety outcomes in a phase 3 study of sunitinib (SU) and FOLFIRI in metastatic colorectal cancer (mCRC). Poster session, Sunday, April 3, 2011: 1:00 -5:00 PM. A. Carrato – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.
[16] AACR Accepted Abstract #1291. A phase 1 open-label single-radiolabeled dose study of PF299804 in healthy male volunteers. Poster session, Sunday, April 3, 2011: 1:00 -5:00 PM. C. Bello – Presenter. American Association for Cancer Research 102nd Annual Meeting 2011. Orlando, FL. April 2-6, 2011.

[17] AACR. Stand Up to Cancer. Available at: http://www.aacr.org/home/public--media/stand-up-to-cancer.aspx. Accessed March 21, 2011.

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