# Pfizer Presents Data from Phase 1b Trial Investigating Utomilumab (a 4-1BB agonist) in Combination with a Checkpoint Inhibitor

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Oral ASCO Presentation Shows Encouraging Safety Data and Increased Support for Novel Immunotherapy Combinations

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Pfizer Inc. (NYSE:PFE) today announced results from a Phase 1b trial of Pfizer’s investigational immunotherapy agent utomilumab (the proposed non-proprietary name for PF-05082566), a 4-1BB (also called CD137) agonist, in combination with pembrolizumab, a PD-1 inhibitor, in patients with advanced solid tumors. This is the first reported study of a 4-1BB agonist combined with a checkpoint inhibitor. Encouraging safety data from the study were shared today as an oral presentation at the 52nd Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago.

“While these are early data, the combination of utomilumab with pembrolizumab demonstrates an encouraging safety profile and an early indication of potential anti-tumor activity across solid tumors,” said Anthony W. Tolcher, M.D., director of clinical research at South Texas Accelerated Research Therapeutics (START) San Antonio. “We believe these results warrant further investigation to confirm whether combining utomilumab with a checkpoint inhibitor may amplify anti-tumor responses.”

Of the 23 patients enrolled in the trial, six had a confirmed complete or partial response. The majority (four of six) of these responses lasted at least six months, with two patients maintaining their response for nearly one year at the time of data cut off. Treatment emergent adverse events were generally mild and did not appear to increase with higher doses of utomilumab, and no dose-limiting toxicity was reported.

“Pfizer believes that bringing the promise of immunotherapies for cancer to more patients will occur through combining agents that work on different pathways within the immune system,” said Chris Boshoff, vice president and head of Early Development, Translational and Immuno-Oncology for Pfizer Oncology. “We are exploring numerous utomilumab combinations in order to better understand its potential role in mobilizing the immune system against difficult-to-treat cancers.”

Pfizer is investigating utomilumab in both hematologic cancers and solid tumors in several planned and ongoing trials. It is being evaluated as a single agent across multiple tumors, in combination with rituximab in lymphoma,1 and in combination with other immunotherapies (e.g., OX40 agonist [PF-04518600], anti-CCR4 [mogamulizumab] and avelumab, an investigational fully human anti-PD-L1 IgG1 monoclonal antibody being developed through an alliance between Merck KGaA, Darmstadt, Germany, and Pfizer) in various solid tumors and hematological malignancies.2,3,4 The mogamulizumab/utomilumab combination is a collaboration with Kyowa Hakko Kirin, Japan.3

About the Study

This Phase 1b dose-escalation study assessed overall safety, pharmacokinetics, pharmacodynamics and anti-tumor activity of utomilumab in combination with pembrolizumab in 23 patients with advanced solid tumors (non-small cell lung, renal cell carcinoma, head and neck, pancreatic, anaplastic thyroid, small-cell lung, colon, sarcoma, thymoma and melanoma). The primary objective was to estimate the maximum tolerated dose and select the recommended Phase 2 dose. Patients received utomilumab (0.45 to 5.0 mg/kg) and pembrolizumab (2 mg/kg) intravenously on day one of 21-day cycles. The number of cycles patients have received across all doses ranged from two to 19, and five patients remain on treatment (maximum dosing is 32 cycles).

The six confirmed responses included two complete responses in one patient with small cell lung cancer and one patient with renal cell carcinoma; partial responses were observed in one patient each with renal cell carcinoma, non-small cell lung cancer, head and neck cancer and anaplastic thyroid cancer. The most common treatment related

adverse events were rash, fatigue, itching, fever, decreased appetite and nausea, with none reported as Grade 3 or 4. No patients discontinued due to treatment related toxicity.

About Utomilumab

Utomilumab (PF-05082566) is a fully human monoclonal antibody (mAb) agonist that selectively binds to 4-1BB (also called CD137), a protein receptor expressed in many cancer-fighting T cells. When a 4-1BB agonist binds to CD137, it has been observed to stimulate and increase the number of T cells, which is believed to accelerate the immune response to attack and kill cancer cells. In preclinical models, utomilumab has shown anti-tumor activity by enhancing T cell mediated immune responses.5,6,7 Utomilumab is being studied in combination with checkpoint inhibitors, which act on another immune signaling pathway and are believed to work by blocking signals from cancer cells which inhibit the host immune system. This signal blockade may allow the host immune system to attack cancer cells.

Learn more about how Pfizer Oncology is applying innovative approaches in an effort to improve the outlook for people living with cancer at http://www.pfizer.com/research/therapeutic_areas/oncology.

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for patients worldwide. Our strong pipeline of biologics and small molecules, 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. 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 us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of June 4, 2016. 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 Pfizer’s oncology portfolio, including utomilumab (PF-05082566), potential combination therapies, the potential of immuno-oncology and clinical development plans, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates as well as the possibility of unfavorable study results, including unfavorable new clinical data and additional analyses of existing clinical data; risks associated with initial data, including the risk that the final results of the Phase Ib for utomilumab and/or additional clinical trials may be different from (including less favorable than) the initial data results and may not support further clinical development; whether and when any applications may be filed with regulatory authorities for utomilumab, combination therapies or other product candidates; whether and when regulatory authorities may approve any such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of utomilumab, combination therapies or other product candidates; 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, 2015 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

1 A Study of PF-05082566 As A Single Agent And In Combination With Rituximab. Available at https://clinicaltrials.gov/ct2/show/NCT01307267?term=PF-05082566&rank=3. Accessed April 25, 2016.

2 A Study of Avelumab In Combination With Other Cancer Immunotherapies In Advanced Malignancies (JAVELIN Medley). Available at https://clinicaltrials.gov/ct2/show/NCT02554812?term=PF-05082566&rank=4. Accessed April 25, 2016.

3 A Study of PF-05082566 In Combination With Mogamulizumab In Patients With Advanced Solid Tumors. Available at https://clinicaltrials.gov/ct2/show/NCT02444793?term=PF-05082566&rank=1. Accessed

April 25, 2016.

4 A Study of 4-1BB Agonist PF-05082566 Plus PD-1 Inhibitor MK-3475 In Patients With Solid Tumors (B1641003/KEYNOTE-0036). Available at https://clinicaltrials.gov/ct2/show/NCT02179918?term=PF-05082566&rank=2 Accessed April 25, 2016.

5 Fisher TS, Kamperschroer C, Oliphant T, et al. Targeting of 4-1BB by monoclonal antibody PF-05082566 enhances T-cell function and promotes anti-tumor activity [published online ahead of print March 11, 2012]. Cancer Immunol Immunother. doi:10.1007/s00262-012-1237-1.

6 Westwood JA, Hunnam TC, Pegram HJ, et al. Routes of delivery for CpG and anti-CD137 for the treatment of orthotopic kidney tumors in mice. PLoS ONE. 2014; 9(5):1-10.

7 West H. Immune checkpoint inhibitors. JAMA Oncol. 2015;1(1):115. doi:10.1001/jamaoncol.2015.0137. Available at http://oncology.jamanetwork.com/article.aspx?articleid=2174768. Accessed April 25, 2016.

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