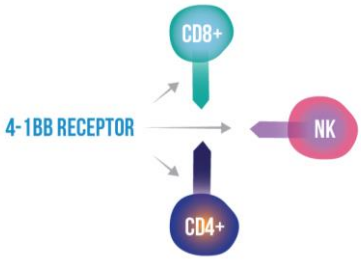
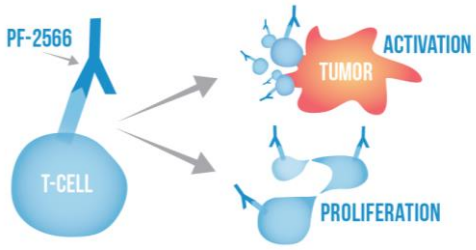
PF-05082566 (4-1BB agonist)

FACT SHEET

PF-05082566 is an investigational agent and has not been approved by regulatory agencies.

ABOUT PF-05082566	PF-05082566 (PF-2566) is an investigational immunotherapy and fully humanized monoclonal antibody (mAb) administered intravenously that stimulates signaling through 4-1BB (CD-137), a protein expressed in many immune cells.
PF-05082566 MECHANISM OF ACTION	The 4-1BB (CD-137) protein receptor is found on T cells such as CD8+ T cells, natural killer cells and CD4+ T cells.[1,2]  Based on pre-clinical data, when PF-2566 binds to 4-1BB, it stimulates and increases the number of immune cells.[1] This may provide enhanced anti-tumor immune function.[1] This is different from checkpoint inhibitors (i.e. PD-1, PD-L1), which act on another immune signaling pathway and are believed to work by inhibiting suppression of T-cells.[3] 
THE POTENTIAL OF A COMBINATION APPROACH	Preclinical studies suggest that combining PF-2566 with a checkpoint inhibitor, such as anti-PD-L1, or other immunotherapies may be able to amplify the immune response.[4,5,6] Further understanding the biology of how the immune system attacks tumors and ways by which tumors evade the immune system may lead to a variety of promising combinations in the future.
CLINICAL STUDIES	Pfizer is exploring the potential of PF-2566 in a clinical development program to determine: (a) the maximum tolerated dose (b) efficacy and (c) therapeutic potential in combination with other therapies. Data from a Phase 1 study that evaluated PF-2566 (4-1BB) in combination with rituximab in patients with relapsed or refractory CD20+ Non-Hodgkin's Lymphoma (NHL) presented at the 2015 ASCO Annual Meeting showed that 4-1BB demonstrated anti-tumor activity.[7] • No dose-limiting toxicities were observed and no patients discontinued treatment due to treatment-related AEs. These results characterize the potential efficacy for this investigational immunotherapy when used in combination with a drug such as rituximab that has a different MOA.[7] Pfizer will further explore 4-1BB in order to better understand its efficacy and safety when used as both a single agent and when used in combination with other anti-cancer therapies, including immunotherapies.

For more information, please visit www.pfizercancertrials.com or www.clinicaltrials.gov or call toll-free 1-877-369-9753 (in the United States and Canada) or +1-646-277-4066 (outside of the United States and Canada).

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[1] 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.

[2] 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.

[3] JAMA Oncol. 2015;1(1):115. doi:10.1001/jamaoncol.2015.0137. Available at http://oncology.jamanetwork.com/article.aspx?articleid=2174768.

[4] Wei H, Zhao L, Li W, et al. Combinatorial PD-1 blockade and CD137 activation has therapeutic efficacy in murine cancer models and synergizes with cisplatin. PLoS ONE. 2013; 8(12):1-11.

[5] Curran MA, Kim M, Montalvo W, et al. Combination CTLA-4 blockage and 4-1BB activation enhances tumor rejection by increasing t-cell infiltration, proliferation, and cytokine production. PLoS ONE. 2011; 6(4):1-11.

[6] Guo Z, Cheng D, Xia Z, et al. Combined TIM-3 blockade and CD137 activation affords the long-term protection in a murine model of ovarian cancer.

[7] J Clin Oncol 33, 2015 (suppl; abstr 3004). Available at http://abstracts.asco.org/156/AbstView_156_147130.html.