



**Epidermal Growth Factor Receptor Variant III (EGFRvIII) Investigational Vaccine (PF-04948568)
(formerly known as CDX-110)**

Fact Sheet

COMPOUND DESCRIPTION	<ul style="list-style-type: none"> • PF-04948568 is an investigational immuno-oncology vaccine targeting the tumor specific epidermal growth factor receptor (EGFR) mutant EGFRvIII. • On April 16, 2008, Pfizer Vaccines LLC. and Celldex Therapeutics, Inc. entered into an agreement that granted Pfizer an exclusive worldwide license to PF-04948568.
MECHANISM OF ACTION	<ul style="list-style-type: none"> • The EGFRvIII protein contains a unique peptide sequence that is not found in wild type EGFR.¹ • This sequence was used to generate the immuno-oncologic peptide molecule, PF-04948568, a 14 amino acid peptide chemically conjugated to Keyhole Limpet Hemocyanin (KLH).² • It is hypothesized that PF-04948568 can induce a tumor specific immune response.³
ABOUT EGFR	<ul style="list-style-type: none"> • The (EGFR) gene is often overexpressed and/or mutated in a variety of tumors⁴, including Glioblastoma Multiforme (GBM), breast cancer, non-small cell lung cancer and ovarian cancer.⁵ • Molecules that promote cell growth (growth factors) or their specific receptors (e.g. EGFR) can be altered in cancer such that they trigger unregulated growth, survival, invasion, and recruitment of new tumor blood vessels.⁶
ABOUT EGFRvIII	<ul style="list-style-type: none"> • EGFRvIII, a functional variant of wild type EGFR, is the most common mutated form of the natural EGFR expressed on tumor cells.⁵ • EGFRvIII is constitutively activated and, by providing a constant growth signal to tumor cells expressing EGFRvIII, can directly contribute to cancer cell growth.⁷ • Unlike wild type EGFR, EGFRvIII is not present in normal tissues,⁸ but may be expressed in a number of cancers and in up to 50% of GBMs.⁹ • The presence of EGFRvIII in malignant cells supports its investigation as a rational, strategic, tumor-specific target for anti-cancer therapy. It also makes it a potential target for active immunization.⁹
CLINICAL STUDIES	<ul style="list-style-type: none"> • ACT III is a single-arm open-label clinical trial. It will enroll a total of 60 patients who will receive PF-04948568. The trial was amended from a 2-arm open-label trial design when it was determined that the majority of patients randomized to the control arm withdrew from the study and the trial could no longer achieve the planned statistical goals.

For additional information, please visit: <http://www.pfizer.com/asco>.

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- ¹ Kuan C-T et al. *EGF Mutant Receptor VIII as a Molecular Target in Cancer Therapy*, Endocrine-Related Cancer, 8, 2008. p.83
- ² Heimberger A, et al. *Epidermal Growth Factor Receptor VIII Peptide Vaccination is Efficacious Against Established Intracerebral Tumors* Clin Cancer Res Vol 9, p.4247, S2003
- ³ Sampson J et al. *Effect of EGFRVIII-targeted vaccine (CDX-110) on immune response and TTP when given with simultaneous standard and continuous temozolomide in patients with GBM*, J Clin Oncol 26; 2008 (May 20 suppl; abstr 2011)
- ⁴ Rude Voldborg B.; Damstrup L.; Spang-Thomsen M.; Skovgaard Poulsen H. *Epidermal growth factor receptor (EGFR) and EGFR mutations, function and possible role in clinical trials* Annals of Oncology, Vol. 8, No. 12, December 1997 , pp. 1197-1206(10)
- ⁵ Kuan C-T et al. *EGF mutant receptor VIII as a molecular target in cancer therapy*, Endocrine-Related Cancer, 8, 2008. p.83
- ⁶ Fonsanto, V. et al. *Expression of Pax2 in Human Renal Tumor-Derived Endothelial Cells Sustains Apoptosis Resistance and Angiogenesis*. American Journal of Pathology, Vol. 168, No. 2, February 2006
- ⁷ Heimberger A. et al. *Prognostic Effect of Epidermal Growth Factor Receptor and EGFR VIII in Glioblastoma Multiforme Patients* Clin Cancer Res Vol 11, p.1462 February 15, 2005
- ⁸ Sok C, et al. *Mutant Epidermal Growth Factor Receptor (EGFRVIII) Contributes to Head and Neck Cancer Growth and Resistance to EGFR Targeting* Clin Cancer Res; 12(17) Sept.1, 2006
- ⁹ Wikstrand C, et al. *Cell Surface Localization and Density of the Tumor-Associated Variant of the Epidermal Growth Factor Receptor, EGFRvII* Cancer Res 57, p.4130, September 15 1997

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