OX40 AGONIST

PF-04518600 (PF-8600) is an investigational, fully human, monoclonal antibody (mAb) immunotherapy that targets the OX40 protein (CD134), a receptor that is expressed on several types of cancer-fighting T cells (types of immune cells).

MECHANISM OF ACTION

OX40 protein is found mostly on memory T cells (CD4+ and CD8+) that have recently been exposed to antigens. When an OX40 agonist, such as PF-8600, binds to the OX40 protein receptor, it triggers a co-stimulatory signal that is associated with increased production of T cells and inflammatory cytokines. This mechanism is thought to activate the dormant immune settings, which then may help fight cancer cells. It may also suppress and/or reduce the regulatory T cells (Treg) that inhibit an immune response.

THE POTENTIAL OF COMBINATION APPROACH

Preclinical studies suggest that combining PF-8600 with a checkpoint inhibitor, such as anti-PD-1/anti-PD-L1, or other immunotherapies may be able to amplify the immune response and show additive activity in syngeneic tumor models. More research, however, is needed to fully understand the mechanism of action of these potential combination approaches.

CLINICAL STUDIES

Pfizer is exploring the potential of PF-8600 OX40 in a clinical development program to determine

- Maximum tolerated dose
- Anti-tumor activity and safety profile
- Therapeutic potential as a monotherapy and in combination with other therapies

The safety and efficacy of the agent(s) under investigation have not been established. There is no guarantee that the agent(s) will receive regulatory approval and become commercially available for use(s) being investigated. All information is current as of June 2017.
**ONGOING STUDIES**

- A first-in-human (FIH) Phase 1 study of PF-8600 agonist in adult patients with select advanced malignancies.¹
- A Phase 1 study as a single agent or in combination with utomilumab (the non-proprietary name for PF-05082566) in select advanced or metastatic carcinomas (NCT02315066).²
- A Phase 1b/2 study in combination with avelumab in patients with locally advanced or metastatic solid tumors, including a triplet combination with avelumab and utomilumab, a CD137 (4-1BB) agonist (NCT02554812).

In addition to the ongoing studies, Pfizer is collaborating with the National Cancer Institute (NCI) under a Cooperative Research and Development Agreement (CRADA) to study three immunotherapy agents, including PF-8600, utomilumab, and avelumab immuno-oncology assets alone and in various combinations targeting multiple cancers.³

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**REFERENCES**


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