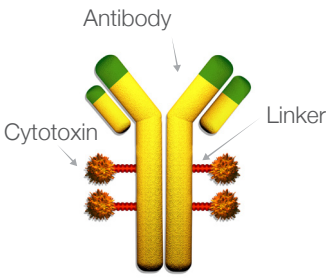
Antibody-Drug Conjugates (ADCs)

Antibody-Drug Conjugates, or ADCs, are designed to precisely deliver cytotoxins to cancer cells with potential to treat both solid tumors and hematologic cancers.

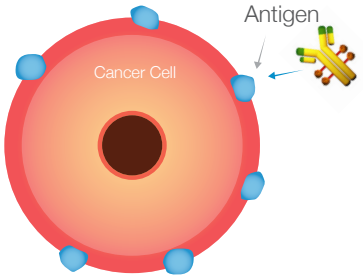
Mechanism of Action

ADCs use a chemical linker to connect cytotoxins – such as chemotherapy – with an antibody. This enables the ADC to target and bind to cell-surface proteins called antigens that can be found on cancer cells and release its cell-killing drugs only after it has been internalized by the cancer cell. As a result, ADCs have the potential to selectively kill cancer cells and limit side effects for patients.

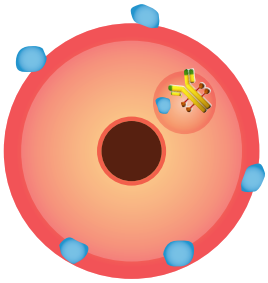
ADCs use a chemical linker to connect cytotoxins with an antibody



ADC binds to antigens



Cytotoxins are released after being internalized by the cancer cell



ADC selectively kills cancer cell

Pfizer ADC Portfolio

Pfizer is using its understanding of the biology of cancer to explore a number of antibody-linker-cytotoxin combinations and build proprietary ADC platforms to develop a diverse ADC toolkit.

Late-Stage Assets

Inotuzumab ozogamicin is an investigational ADC comprised of a CD22-directed mAb linked to the cytotoxic agent calicheamicin and is being studied in relapsed/refractory acute lymphoblastic leukemia (ALL)

MYLOTARG (gemtuzumab ozogamicin) is an ADC comprised of a CD33-directed mAb that is linked to the cytotoxic agent calicheamicin and has been studied in acute myeloid leukemia (AML).*

Early-Stage Investigational Assets

PF-06650808 is an **anti-NOTCH3 ADC** that is comprised of a humanized antibody targeting the NOTCH3 receptor, which is overexpressed in a number of human cancers, linked to an auristatin-based cytotoxic agent.

In a Phase 1 study **PF-06650808 (anti-Notch3)** showed an acceptable safety profile in patients with advanced malignancies, including triple negative breast cancer, ovarian cancer and non-small cell lung cancer.[1] **PF-06650808** also showed early indication of anti-tumor activity in an unselected patient population.

PF-06647020 is an **anti-PTK7 ADC** that is comprised of a humanized monoclonal antibody directed against PTK7, which is also expressed in many tumor types, linked to an auristatin microtubule inhibitor payload.

In a Phase 1 study **PF-06647020 (anti-PTK7)** showed an acceptable safety profile in patients with advanced malignancies, including triple negative breast cancer, ovarian cancer and non-small cell lung cancer **PF-06647020** also showed early indication of anti-tumor activity in an unselected patient population.[2]

PF-06647263 is an **anti-EFNA4 ADC** that is comprised of a humanized monoclonal antibody against Ephrin-A4 (EFNA4), which is overexpressed in a number of human tumors, linked to the cytotoxic agent calicheamicin.

In a Phase 1 study **PF-06647263 (anti-EFNA4)** showed an acceptable safety profile in patients with advanced malignancies, including triple negative breast cancer and ovarian cancer.[3] Results showed early indication of anti-tumor activity in an unselected patient population.

* = MYLOTARG is not approved in the U.S.

[1] Rosen, L.S., et al. 30LBA A Phase 1 dose escalation, safety, and pharmacokinetic study of PF-06650808, an anti-Notch3 antibody drug conjugate, in adult patients with advanced solid tumors. European Journal of Cancer. DOI: 10.1016/S0959-8049(16)31948-7.

[2] Tolcher, A.W., et al. 28LBA A Phase 1 study of PF-06647020, an antibody-drug conjugate targeting PTK7, in patients with advanced solid tumors. European Journal of Cancer. DOI: 10.1016/S0959-8049(16)31946-3.

[3] Hong, D.S., et al. First-in-human dose escalation, safety, and PK study of a novel EFNA4-ADC in patients with advanced solid tumors. J Clin Oncol (Meeting Abstracts) 2015: 2520. Available at: http://meeting.ascopubs.org/cgi/content/abstract/33/15_suppl/2520. Accessed April 1, 2015. NCT02078752?term=PF-06647263&rank=1. Accessed March 22, 2016.