

# Genentech **FACT SHEET**



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## **Pipeline: Insight and Innovation from Genentech BioOncology**

As a result of our commitment to basic research, Genentech BioOncology has a robust product pipeline, with innovative compounds designed to target cancer via specific molecular processes. We believe that studying the biological pathways involved in cancer development, progression and metastasis holds the key to identifying promising molecular targets.

Genentech BioOncology also supports the development of clinical diagnostics to identify patients most likely to benefit from treatment with our medicines. Scientists at Genentech are investigating potential diagnostic markers, including HER receptors, that may aid selection of the patients most likely to benefit from our targeted therapies.

Through our current research focus, including angiogenesis, cell signaling (HER signaling, apoptosis and B-cell signaling) and arming antibodies, we approach cancer research from multiple pathways, helping us to unravel the complexity of cancer and to develop targeted therapies that will address the unmet needs of cancer treatment and positively impact the lives of patients.

Genentech BioOncology's pipeline includes both innovations and new indications for existing products that may fight more than one disease or more than one form of a disease. While we are studying Avastin<sup>®</sup>, Herceptin<sup>®</sup>, Rituxan<sup>®</sup> and Tarceva<sup>®</sup> in numerous new oncology indications as well as conducting combination trials, we are also investigating several new molecules as cancer therapies, including:

- Apomab
- RhApo2L/TRAIL (recombinant human Apo2 ligand/tumor necrosis factor-related apoptosis-inducing ligand), in collaboration with Amgen
- Pertuzumab
- Trastuzumab-DM1 (T-DM1)

### **Apomab and RhApo2L/TRAIL: Cell Signaling/Apoptosis**

Apoptosis, or "programmed cell death," is a process by which cells in the body, both normal and abnormal, self-destruct. Under normal conditions, apoptosis eliminates damaged or unneeded cells.<sup>1</sup> However, many cancer cells evade apoptosis, allowing tumors to survive and grow.<sup>2</sup> Therefore, developing therapies that can activate – or induce – apoptosis may have the potential for treating a variety of cancers.<sup>3</sup>

### **Apomab**

Apomab is a fully human antibody discovered by Genentech scientists that is designed to specifically bind to and activate an important receptor, called pro-apoptotic receptor DR5, which is found on the surface of various types of cancer cells.<sup>4</sup>

Binding of Apomab to DR5 may directly activate the extrinsic apoptosis pathway as well as may indirectly induce the intrinsic apoptosis pathway in cancer cells.<sup>5</sup> In preclinical models, Apomab selectively induced apoptosis in cancer cells, while sparing normal cells.<sup>5,6</sup>

Genentech scientists are currently studying Apomab in early-stage clinical trials in a variety of solid tumors and blood cancers. In April 2007, Genentech announced the initiation of two Apomab Phase II clinical studies, one in non-small cell lung cancer and the other in non-Hodgkin's lymphoma (NHL).

### **Recombinant Human (Rh)Apo2L/TRAIL**

Apo2 ligand/tumor necrosis factor-related apoptosis-inducing ligand (Apo2L/TRAIL) is a recombinant (engineered) human protein designed to activate both pro-apoptotic receptors, DR4 and DR5.<sup>4</sup>

Binding of rhApo2L/TRAIL to DR4 and DR5 may directly activate the extrinsic apoptosis pathway as well as may indirectly induce the intrinsic apoptosis pathway in cancer cells.<sup>7-9</sup> In preclinical models, rhApo2L/TRAIL selectively induced apoptosis in cancer cells, while sparing normal cells.<sup>8</sup>

Genentech BioOncology, in collaboration with Amgen, is studying rhApo2L/TRAIL, the first dual pro-apoptotic receptor agonist, in early-stage clinical trials in a variety of solid tumors and blood cancers, including a Phase II study in NHL.

### **Pertuzumab: Cell-Signaling**

Pertuzumab, a humanized monoclonal antibody, represents the first in a new class of investigational agents known as HER (human epidermal growth factor receptor) dimerization inhibitors (HDIs).<sup>10</sup>

Pertuzumab is designed to bind to the HER2 receptor – a protein found on the surface of epithelial cells – and inhibits the ability of HER2 to interact with other HER family members (HER1/EGFR, HER2, HER3, and HER4).<sup>11,12</sup> HER dimerization (receptor pairing) is believed to play an important role in the growth and formation of several different cancer types.<sup>10</sup>

Pertuzumab binds to a different part of the HER2 receptor than other approved products, known as the dimerization domain.

Due to its potential to inhibit HER family members from pairing, it is believed pertuzumab may be applicable in a variety of solid tumors, including those that are HER2-positive and those that do not overexpress HER2.<sup>10,13,14</sup>

Genentech recently announced a decision to initiate a Phase III clinical development program investigating pertuzumab for the treatment of first-line, HER2-positive metastatic breast cancer. Genentech continues to further analyze the results from a Phase II study evaluating pertuzumab in combination with gemcitabine in ovarian cancer.

### **Trastuzumab-DM1 (T-DM1): Armed Antibody**

T-DM1 is a first-in-class investigational HER2 antibody drug conjugate consisting of a potent cancer-killing drug linked to the HER2-specific monoclonal antibody trastuzumab.<sup>15,16</sup> T-DM1 is being studied in Phase I clinical trials in patients with locally advanced or metastatic HER2-positive breast cancer who have progressed on a chemotherapy regimen containing Herceptin. A Phase II trial is planned.

For the full prescribing information for Tarceva and the full prescribing information and Boxed Warnings for Rituxan, Herceptin, and Avastin please visit <http://www.gene.com>.

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