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## Pertuzumab Fact Sheet

### About Pertuzumab

- Pertuzumab, an investigational monoclonal antibody being studied in early-stage and advanced HER2-positive breast cancer, is a targeted medicine known as a “HER2 dimerization inhibitor” (HDI).
- In breast cancer, approximately 20-30 percent of tumors strongly overexpress the HER2 protein on the surface of cancer cells, which is known as HER2-positive breast cancer.<sup>1</sup>
- Pertuzumab is designed to block the ability of the HER2 protein to pair (dimerize) with other proteins in the HER family (HER1, HER2, HER3 or HER4).<sup>2</sup> By doing this, it is thought to inhibit the growth of the tumor.<sup>2</sup>

### HER2 Dimerization

- Through dimerization, a HER2 protein pairs with another HER2 protein or with another protein in the HER family. These dimers initiate signals that stimulate tumor cell growth and survival.
- Pairing between HER2 and HER3 is believed to be especially important for HER2-positive breast cancer tumor cell growth and survival.<sup>3,4,5,6</sup>

### How Pertuzumab May Work

- Pertuzumab is being studied in combination with other targeted medicines, including Herceptin<sup>®</sup> (trastuzumab) and the investigational medicine T-DM1.
- Pertuzumab and Herceptin both bind to distinct parts of the HER2 protein and are believed to have complementary mechanisms of action.<sup>7,8,9,10,11</sup>
- Herceptin is thought to bind to a region on the HER2 protein and block certain processes involved in tumor growth, while pertuzumab is designed to work by preventing HER2 dimerization, especially pairing between HER2 and HER3. This more comprehensive HER2 blockade provided by pertuzumab and Herceptin together may potentially inhibit cell growth and may result in tumor shrinkage.
- In addition, both pertuzumab and Herceptin may engage the body’s immune system to attack tumor cells.
- In preclinical studies, combining pertuzumab and Herceptin resulted in greater tumor growth inhibition than with either medicine alone.

### Ongoing Pertuzumab Clinical Studies

- NEOSPHERE, a Phase II trial of pertuzumab in combination with Herceptin and chemotherapy for treating early-stage HER2-positive breast cancer prior to surgery (neoadjuvant setting). Results will be presented in 2010.
- CLEOPATRA, a Phase III trial of pertuzumab in combination with Herceptin and chemotherapy for first-line treatment of advanced HER2-positive breast cancer. Results are expected in 2011.
- MARIANNE, a Phase III trial that includes the combination of pertuzumab and the investigational medicine T-DM1 for first-line treatment of advanced HER2-positive breast cancer.

### About Herceptin

Herceptin is a targeted medicine (not a chemotherapy) designed to specifically block the HER2 protein on the surface of some cancer cells. Based on preclinical studies, Herceptin may work by attaching to HER2 receptors to stop signals that make the tumor cells grow and divide, and also by signaling the body's immune system to destroy the cancer cells.

#### Adjuvant Breast Cancer:

Herceptin is approved for the treatment of early-stage breast cancer that is **H**uman **E**pidermal growth factor **R**eceptor **2**-positive (HER2+) and has spread into the lymph nodes, or is HER2+ and has not spread into the lymph nodes. If it has not spread into the lymph nodes, the cancer needs to be estrogen receptor/progesterone receptor (ER/PR)-negative or have one high risk feature.\* Herceptin can be used in several different ways:

- As part of a treatment course including the chemotherapy drugs doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel. This treatment course is known as "**AC→TH**"
- With the chemotherapy drugs docetaxel and carboplatin. This treatment course is known as "**TCH**"
- Alone after treatment with multiple other therapies, including an anthracycline-based therapy (a type of chemotherapy)

\*High risk is defined as ER/PR-positive with one of the following features: tumor size >2 cm, age <35 years, or tumor grade 2 or 3.

#### Metastatic Breast Cancer:

Herceptin has two approved uses in metastatic breast cancer:

- Herceptin in combination with the chemotherapy drug paclitaxel is approved for the first line treatment of **H**uman **E**pidermal growth factor **R**eceptor **2**-positive (HER2+) metastatic breast cancer
- Herceptin alone is approved for the treatment of HER2+ breast cancer in patients who have received one or more chemotherapy courses for metastatic disease

Metastatic Gastric Cancer:

Herceptin is approved in combination with the chemotherapy drugs cisplatin, and either capecitabine or 5-fluorouracil, for metastatic HER2-positive stomach cancer or cancer of the gastroesophageal junction, in men and women who have not received prior medicines for their metastatic disease.

### **Important Safety Information Including Serious Side Effects**

**Herceptin treatment can result in heart problems, including those without symptoms (such as reduced heart function) and those with symptoms (such as congestive heart failure). One patient died in an adjuvant (early) breast cancer trial from significantly weakened heart muscle. The risk and seriousness of these heart problems were highest in people who received both Herceptin and a certain type of chemotherapy (anthracycline).**

Before taking the first dose of Herceptin and during treatment, a patient's doctor should check to see if there are any health conditions that may increase the patient's chance of having serious heart problems. This includes a review of the patient's health history and tests to see how well the heart muscle is working. These tests may include an echocardiogram or a MUGA scan. Some early breast cancer patients may also need to have a test done after they have finished taking Herceptin to see how well their heart muscle is working.

**Some patients have had serious infusion reactions and lung problems; fatal infusion reactions have been reported. These reactions usually occur during or within 24 hours of receiving Herceptin.**

**The patient's doctor may need to completely stop Herceptin treatment if the patient has a severe allergic reaction, swelling, lung problems, inflammation of the lung, or severe shortness of breath.**

**Herceptin can cause harm to the fetus (unborn baby), in some cases death to the fetus, when taken by a pregnant woman.** Women who could become pregnant need to use effective birth control methods during Herceptin treatment and for at least 6 months after treatment with Herceptin. Nursing mothers treated with Herceptin should discontinue nursing or discontinue Herceptin.

Worsening of low white blood cell counts associated with chemotherapy has also occurred.

Patients must have a HER2 test to determine if their breast or stomach cancer is HER2-positive before using Herceptin, as benefit has only been shown in patients that are HER2-positive.

The most common side effects associated with Herceptin in patients with breast cancer are fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue, shortness of breath, rash, low white and red blood cells, and muscle pain.

The most common side effects associated with Herceptin in patients with stomach cancer are low white blood cell counts, diarrhea, fatigue, low red blood cell counts, inflammation of the lining of the mouth, weight loss, upper respiratory tract infections, fever, low platelet counts, swelling of mucus membranes, swelling of the nose and throat, and a change in taste.

Because everyone is different, it is not possible to predict what side effects any one person will have. Patients with questions or concerns about side effects should talk to their doctor.

Patients should read the Herceptin Full Prescribing Information including Boxed WARNINGS, at [www.herceptin.com](http://www.herceptin.com).

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<sup>7</sup> Cho HS et al. Structure of the extracellular region of HER2 alone and in complex with the Herceptin Fab. *Nature* 2003;421:756–760

<sup>8</sup> Fendly BM et al. Characterization of murine monoclonal antibodies reactive to either the human epidermal growth factor receptor or HER2/neu gene product. *Cancer Research* 1990;50:1550–1558

<sup>9</sup> Nahta R et al. The HER-2-Targeting Antibodies Trastuzumab and Pertuzumab Synergistically Inhibit the Survival of Breast Cancer Cells. *Cancer Research* 2004;64:2343–2346

<sup>10</sup> Rajasekaran R and Rao S. Comparative binding analysis of monoclonal antibodies against native and mutant type in ErbB2 receptor: a theoretical modeling approach. *Current Pharmaceutical Biotechnology* 2009;10:701–708

<sup>11</sup> Scheuer W et al. Strongly enhanced antitumor activity of trastuzumab and pertuzumab combination treatment on HER2-positive human xenograft tumor models. *Cancer Research* 2009;69:9330–9336

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