



## **FDA Approves Amgen And Allergan's KANJINTI™ (trastuzumab-anns), A Biosimilar To Herceptin® (trastuzumab)**

June 13, 2019

### **Approval Based on Totality of Evidence Demonstrating KANJINTI is Biosimilar to Herceptin Third FDA Approval From Amgen's Biosimilars Portfolio**

THOUSAND OAKS, Calif., June 13, 2019 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and Allergan plc (NYSE:AGN) today announced that the U.S. Food and Drug Administration (FDA) has approved KANJINTI™ (trastuzumab-anns) for all approved indications of the reference product, Herceptin® (trastuzumab): for the treatment of HER2-overexpressing adjuvant and metastatic breast cancer and HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

"The FDA approval of KANJINTI is an important milestone for our biosimilars portfolio, providing an additional treatment option for patients across three types of cancer," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "KANJINTI is the third biosimilar from our portfolio to receive FDA approval, highlighting our long-term commitment to providing patients with serious illnesses access to high-quality biological therapies."

KANJINTI was proven to be highly similar to, and to have no clinically meaningful differences from, Herceptin based on a comprehensive totality of evidence which included extensive comparative analytical, pharmacokinetic and clinical data. At the time of approval, KANJINTI is the only trastuzumab biosimilar to incorporate the evaluation of a single transition in the clinical study, demonstrating similar safety and immunogenicity in patients who were previously on Herceptin.

"KANJINTI is the second of four biosimilars from Amgen and Allergan's collaboration to be approved by the FDA," said David Nicholson, chief research and development officer at Allergan. "We are proud of the progress being made as we continuously strive to develop and deliver high-quality cancer therapies in collaboration with Amgen."

Amgen has a total of 10 biosimilars in its portfolio, three of which have been approved in the U.S. and three that are approved in the European Union (EU).

#### **About KANJINTI™ (trastuzumab-anns) in the U.S.**

KANJINTI is a biosimilar to trastuzumab, a recombinant DNA-derived humanized monoclonal immunoglobulin G1 kappa antibody. The active ingredient of KANJINTI is a humanized monoclonal antibody that has the same amino acid sequence, structure and function as trastuzumab. KANJINTI has the same pharmaceutical dosage form and same strength after reconstitution as trastuzumab.

KANJINTI is currently not available commercially. This is not an offer for sale. The following information is derived from the approved label in the U.S.

In the U.S., KANJINTI is approved for:

#### **Adjuvant Breast Cancer**

KANJINTI is indicated for adjuvant treatment of HER2-overexpressing node-positive or node-negative (ER/PR-negative or with one high-risk feature\*) breast cancer:

- As part of a treatment regimen containing doxorubicin, cyclophosphamide and either paclitaxel or docetaxel
- With docetaxel and carboplatin
- As a single agent following multi-modality anthracycline-based therapy

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

\* 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**

KANJINTI is indicated:

- In combination with paclitaxel for the first line treatment of HER2-overexpressing metastatic breast cancer
- As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

#### **Metastatic Gastric Cancer**

KANJINTI is indicated, in combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease.

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

#### **KANJINTI U.S. Boxed WARNINGS and Important Safety Information**

#### **Boxed WARNINGS and Additional Important Safety Information Cardiomyopathy**

- Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens
- Evaluate left ventricular function in all patients prior to and during treatment with KANJINTI™. Discontinue KANJINTI™ treatment in patients receiving adjuvant therapy and withhold KANJINTI™ in patients with metastatic disease for clinically significant decrease in left ventricular function

#### Infusion Reactions; Pulmonary Toxicity

- Administration of trastuzumab products can result in serious and fatal infusion reactions and pulmonary toxicity. Symptoms usually occur during or within 24 hours of administration. Interrupt KANJINTI™ infusion for dyspnea or clinically significant hypotension. Monitor patients until symptoms completely resolve. Discontinue KANJINTI™ for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome

#### Embryo-Fetal Toxicity

- Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception

#### Cardiomyopathy

- Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens. In a pivotal adjuvant breast cancer trial, one patient who developed CHF died of cardiomyopathy
- Trastuzumab can cause left ventricular cardiac dysfunction, arrhythmias, hypertension, disabling cardiac failure, cardiomyopathy, and cardiac death
- Trastuzumab can also cause asymptomatic decline in LVEF
- Discontinue KANJINTI™ treatment in patients receiving adjuvant breast cancer therapy and withhold KANJINTI™ in patients with metastatic disease for clinically significant decrease in left ventricular function

#### Cardiac Monitoring

- Evaluate cardiac function prior to and during treatment. For adjuvant breast cancer therapy, also evaluate cardiac function after completion of KANJINTI™
- Conduct thorough cardiac assessment, including history, physical examination, and determination of LVEF by echocardiogram or MUGA scan
- Monitor frequently for decreased left ventricular function during and after KANJINTI™ treatment
- Monitor more frequently if KANJINTI™ is withheld for significant left ventricular cardiac dysfunction

#### Infusion Reactions

- KANJINTI™ administration can result in serious and fatal infusion reactions
- Symptoms usually occur during or within 24 hours of KANJINTI™ administration
- Interrupt KANJINTI™ infusion for dyspnea or clinically significant hypotension
- Monitor patients until symptoms completely resolve
- Discontinue KANJINTI™ for infusion reactions manifesting as anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. Strongly consider permanent discontinuation in all patients with severe infusion reactions
- Infusion reactions consist of a symptom complex characterized by fever and chills, and on occasion include nausea, vomiting, pain (in some cases at tumor sites), headache, dizziness, dyspnea, hypotension, rash, and asthenia

#### Embryo-Fetal Toxicity

- Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception
- Verify the pregnancy status of females of reproductive potential prior to the initiation of KANJINTI™
- Advise pregnant women and females of reproductive potential that exposure to KANJINTI™ during pregnancy or within 7 months prior to conception can result in fetal harm
- Advise females of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose of KANJINTI™. Advise female patients to contact their healthcare provider with a known or suspected pregnancy
- Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for KANJINTI™ treatment and any potential adverse effects on the breastfed child from KANJINTI™ or from the underlying maternal

condition

### **Pulmonary Toxicity**

- **Trastuzumab products can result in serious and fatal pulmonary toxicity**, which includes dyspnea, interstitial pneumonitis, pulmonary infiltrates, pleural effusions, noncardiogenic pulmonary edema, pulmonary insufficiency and hypoxia, acute respiratory distress syndrome, and pulmonary fibrosis. Such events can occur as sequelae of infusion reactions
- Patients with symptomatic intrinsic lung disease or with extensive tumor involvement of the lungs, resulting in dyspnea at rest, appear to have more severe toxicity
- Discontinue KANJINTI™ in patients experiencing pulmonary toxicity

### **Exacerbation of Chemotherapy-Induced Neutropenia**

- In randomized, controlled clinical trials, the per-patient incidences of NCI-CTC Grade 3-4 neutropenia and of febrile neutropenia were higher in patients receiving trastuzumab in combination with myelosuppressive chemotherapy as compared to those who received chemotherapy alone. The incidence of septic death was similar among patients who received trastuzumab and those who did not

### **Most Common Adverse Reactions**

- The most common adverse reactions associated with trastuzumab products in breast cancer were fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue, dyspnea, rash, neutropenia, anemia, and myalgia
- The most common adverse reactions associated with trastuzumab products in metastatic gastric cancer were neutropenia, diarrhea, fatigue, anemia, stomatitis, weight loss, upper respiratory tract infections, fever, thrombocytopenia, mucosal inflammation, nasopharyngitis, and dysgeusia

You may report side effects to the FDA at (800) FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch). You may also report side effects to Amgen at 1-800-772-6436. Please see additional select Important Safety Information throughout, and the accompanying [full Prescribing Information](#), including **Boxed WARNINGS**.

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### **About the Amgen and Allergan Collaboration**

In December 2011, Amgen and Allergan plc. (then Watson Pharmaceuticals, Inc.) formed a collaboration to develop and commercialize, on a worldwide basis, four oncology antibody biosimilar medicines. This collaboration reflects the shared belief that the development and commercialization of biosimilar products will not follow a pure brand or generic model and will require significant expertise, infrastructure, and investment to ensure safe, reliably supplied therapies for patients. Under the terms of the agreement, Amgen will assume primary responsibility for developing, manufacturing and initially commercializing the oncology antibody products.

### **About Amgen Biosimilars**

Amgen is committed to building upon Amgen's experience in the development and manufacturing of innovative human therapeutics to expand Amgen's reach to patients with serious illnesses. Biosimilars will help to maintain Amgen's commitment to connect patients with vital medicines, and Amgen is well positioned to leverage its nearly four decades of experience in biotechnology to create high-quality biosimilars and reliably supply them to patients worldwide.

For more information, visit [www.amgenbiosimilars.com](http://www.amgenbiosimilars.com) and follow us on [www.twitter.com/amgenbiosim](https://www.twitter.com/amgenbiosim).

### **About Amgen Oncology**

Amgen Oncology is searching for and finding answers to incredibly complex questions that will advance care and improve lives for cancer patients and their families. Our research drives us to understand the disease in the context of the patient's life – not just their cancer journey – so they can take control of their lives.

For the last four decades, we have been dedicated to discovering the firsts that matter in oncology and to finding ways to reduce the burden of cancer. Building on our heritage, Amgen continues to advance the largest pipeline in the Company's history, moving with great speed to advance those innovations for the patients who need them.

At Amgen, we are driven by our commitment to transform the lives of cancer patients and keep them at the center of everything we do.

For more information, follow us on [www.twitter.com/amgenoncology](https://www.twitter.com/amgenoncology).

### **About Amgen**

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit [www.amgen.com](http://www.amgen.com) and follow us on [www.twitter.com/amgen](https://www.twitter.com/amgen).

### **About Allergan plc**

Allergan plc (NYSE: AGN), headquartered in Dublin, Ireland, is a bold, global pharmaceutical leader. Allergan is focused on developing, manufacturing and commercializing branded pharmaceutical, device, biologic, surgical and regenerative medicine products for patients around the world.

Allergan markets a portfolio of leading brands and best-in-class products primarily focused on four key therapeutic areas including central nervous system, eye care, medical aesthetics and gastroenterology.

Allergan is an industry leader in Open Science, a model of research and development, which defines our approach to identifying and developing game-changing ideas and innovation for better patient care. With this approach, Allergan has built one of the broadest development pipelines in the pharmaceutical industry.

Allergan's success is powered by our global colleagues' commitment to being Bold for Life. Together, we build bridges, power ideas, act fast and drive results for our customers and patients around the world by always doing what is right.

With commercial operations in approximately 100 countries, Allergan is committed to working with physicians, healthcare providers and patients to deliver innovative and meaningful treatments that help people around the world live longer, healthier lives every day.

For more information, visit Allergan's website at [www.Allergan.com](http://www.Allergan.com).

### **Amgen Forward-Looking Statements**

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including its most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those Amgen projects. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for Amgen to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints Amgen has selected. Amgen develops product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with its products, including its devices, after they are on the market.

Amgen's results may be affected by its ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing its products and global economic conditions. In addition, sales of Amgen's products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, Amgen's research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Amgen's business may be impacted by government investigations, litigation and product liability claims. In addition, Amgen's business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Further, while Amgen routinely obtains patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors, or Amgen may fail to prevail in present and future intellectual property litigation. Amgen performs a substantial amount of its commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depends on third parties for a portion of its manufacturing activities, and limits on supply may constrain sales of certain of its current products and product candidate development. Amgen relies on collaborations with third parties for the development of some of its product candidates and for the commercialization and sales of some of its commercial products. In addition, Amgen competes with other companies with respect to many of its marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for Amgen's products are supplied by sole third-party suppliers. Certain of Amgen's distributors, customers and payers have substantial purchasing leverage in their dealings with Amgen. The discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on its business and results of operations. Amgen's efforts to acquire other companies or products and to integrate the operations of companies Amgen has acquired may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of Amgen's systems and Amgen's data. Amgen's stock price may be volatile and may be affected by a number of events. Amgen's business performance could affect or limit the ability of the Amgen Board of Directors to declare a dividend or its ability to pay a dividend or repurchase its common stock. Amgen may not be able to access the capital and credit markets on terms that are favorable to it, or at all.

### **Allergan plc Forward-Looking Statement**

Statements contained in this press release that refer to future events or other non-historical facts are forward-looking statements that reflect Allergan's current perspective on existing trends and information as of the date of this release. Actual results may differ materially from Allergan's current expectations depending upon a number of factors affecting Allergan's business. These factors include, among others, the difficulty of predicting the timing or outcome of FDA approvals or actions, if any; the impact of competitive products and pricing; market acceptance of and continued demand for Allergan's products; the impact of uncertainty around timing of generic entry related to key products, including RESTASIS<sup>®</sup>, on our financial results;

risks associated with divestitures, acquisitions, mergers and joint ventures; risks related to impairments; uncertainty associated with financial projections, projected cost reductions, projected debt reduction, projected synergies, restructurings, increased costs, and adverse tax consequences; difficulties or delays in manufacturing; and other risks and uncertainties detailed in Allergan's periodic public filings with the Securities and Exchange Commission, including but not limited to Allergan's Annual Report on Form 10-K for the year ended December 31, 2018 and Allergan's Quarterly Report on Form 10-Q for the period ended March 31, 2019. Except as expressly required by law, Allergan disclaims any intent or obligation to update these forward-looking statements.

Herceptin® is registered trademark of Genentech, Inc.

CONTACT: Amgen, Thousand Oaks  
Kelley Davenport, 202-585-9637 (media)  
Kristen Davis, 805-447-3008 (media)  
Arvind Sood, 805-447-1060 (investors)

CONTACT: Allergan plc.  
Daphne Karydas, 862-261-8006 (investor relations)  
Amy Rose, 862-261-7001 (media relations)

The logo for Amgen, featuring the word "AMGEN" in a bold, blue, sans-serif font with a registered trademark symbol (®) to the upper right.

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