European Commission Approves Amgen And Allergan's MVASI® (Biosimilar Bevacizumab) For The Treatment Of Certain Types Of Cancer

January 18, 2018

Marketing Authorization Based on Global Development Program Showing MVASI is Highly Similar to Avastin® (Bevacizumab)

First Biosimilar Bevacizumab Approved in the European Union

THOUSAND OAKS, Calif., Jan. 18, 2018 /PRNewswire/ -- Amgen (NASDAQ: AMGN) and Allergan plc. (NYSE: AGN) today announced that the European Commission (EC) has granted marketing authorization for MVASI® (biosimilar bevacizumab). MVASI is the first biosimilar bevacizumab approved by the EC and is approved for the treatment of certain types of cancers, including in combination with fluoropyrimidine-based chemotherapy for metastatic carcinoma of the colon or rectum; in combination with paclitaxel for metastatic breast cancer; in combination with platinum-based chemotherapy for unresectable advanced, metastatic or recurrent non-squamous non-small cell lung cancer (NSCLC); in combination with erlotinib for unresectable advanced, metastatic or recurrent non-squamous NSCLC; in combination with interferon alfa-2a for advanced and/or metastatic renal cell cancer; in combination with carboplatin and paclitaxel, carboplatin and gemcitabine, and paclitaxel, topotecan, or pegylated liposomal doxorubicin for advanced, platinum-sensitive, or platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer; and in combination with paclitaxel and cisplatin, or alternatively, paclitaxel and topotecan for persistent, recurrent, or metastatic carcinoma of the cervix.

"The European Commission's approval of MVASI marks a significant milestone for both Amgen and the oncology community, providing a biosimilar for a medicine which is used across multiple types of cancer," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "MVASI is the first targeted cancer biosimilar from Amgen's portfolio approved in Europe, underscoring our commitment to delivering high-quality medicines that address some of the most serious illnesses."

Amgen and Allergan are committed to developing high-quality biosimilars with a robust analytic and clinical package. The EC approved MVASI based on a comprehensive data package that demonstrated MVASI and bevacizumab are highly similar, with no clinically meaningful differences in terms of the efficacy, safety and immunogenicity between the products. Clinical studies included results from a Phase 3 trial in patients with non-squamous NSCLC.

"MVASI is the first product from our collaboration with Amgen to receive marketing authorization from the European Commission, highlighting the success of our joint commitment to developing cancer biosimilars," said David Nicholson, chief research and development officer at Allergan. "We look forward to our continued work with Amgen and to providing important medicines to patients in the future."

Approval from the EC grants a centralized marketing authorization with unified labeling in the 28 countries that are members of the European Union (EU). Norway, Iceland and Liechtenstein, as members of the European Economic Area, will take corresponding decisions on the basis of the decision of the EC.

In September 2017, MVASI became the first anti-cancer biosimilar, as well as the first biosimilar bevacizumab, to be approved by the U.S. Food and Drug Administration (FDA). Amgen and Allergan are collaborating on the development and commercialization of four oncology biosimilars. Amgen has a total of 10 biosimilars in its portfolio, two of which have been approved by the EC.

About MVASI® (biosimilar bevacizumab) in the EU

MVASI is a biosimilar to bevacizumab, a recombinant immunoglobulin G1 (IgG1) monoclonal antibody (mAb) that binds to vascular endothelial growth factor (VEGF) and inhibits the interaction of VEGF with its receptors, VEGF receptor-1 and VEGF receptor-2, thus inhibiting establishment of new blood vessels necessary for the maintenance and growth of solid tumors.

MVASI, in combination with fluoropyrimidine-based chemotherapy, is indicated for treatment of adult patients with metastatic carcinoma of the colon or rectum.

MVASI, in combination with paclitaxel, is indicated for first-line treatment of adult patients with metastatic breast cancer.

MVASI, in addition to platinum-based chemotherapy, is indicated for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent NSCLC other than predominantly squamous cell histology.

MVASI, in combination with erlotinib, is indicated for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-squamous NSCLC with Epidermal Growth Factor Receptor (EGFR) activating mutations.

MVASI, in combination with interferon alfa-2a, is indicated for first-line treatment of adult patients with advanced and/or metastatic renal cell cancer.

MVASI, in combination with carboplatin and paclitaxel, is indicated for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages IIIB, IIIC and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer.

MVASI, in combination with carboplatin and gemcitabine or in combination with carboplatin and paclitaxel, is indicated for treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor-targeted agents.

MVASI, in combination with paclitaxel, topotecan, or pegylated liposomal doxorubicin, is indicated for the treatment of adult patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than two prior chemotherapy regimens and who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor-targeted agents.

MVASI, in combination with paclitaxel and cisplatin or, alternatively, paclitaxel and topotecan in patients who cannot receive platinum therapy, is indicated for the treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix.

MVASI EU Important Safety Information

The EU Summary of Product Characteristics for MVASI lists the following Special Warnings and Precautions: gastrointestinal (GI) perforations and fistulae, GI-vaginal fistulae in study GOG-0240, non-GI fistulae, wound healing complications, hypertension, posterior reversible encephalopathy syndrome (PRES), proteinuria, arterial thromboembolism, venous thromboembolism, haemorrhage, pulmonary haemorrhage/haemoptysis, congestive heart failure (CHF), neutropenia and infections, hypersensitivity reactions/infusion reactions, osteonecrosis of the jaw (ONJ), intravitreal use, eye disorders, systemic effects following intravitreal use, and ovarian failure/fertility.

About MVASI™ (bevacizumab-awwb) in the U.S.

MVASI is a biosimilar to bevacizumab, a recombinant IgG1 mAb that binds to VEGF and inhibits the interaction of VEGF with its receptors, VEGF receptor-1 and VEGF receptor-2, thus inhibiting establishment of new blood vessels necessary for the maintenance and growth of solid tumors.

MVASI is indicated for the treatment of metastatic colorectal cancer (mCRC), with intravenous 5-fluorouracil–based chemotherapy for first- or second-line treatment.

MVASI is indicated for the treatment of mCRC, with fluoropyrimidine- irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab-containing regimen. MVASI is not indicated for adjuvant treatment of colon cancer.

MVASI is indicated for the treatment of non-squamous NSCLC, with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease.

MVASI is indicated for the treatment of glioblastoma, as a single agent for adult patients with progressive disease following prior therapy.

The effectiveness of bevacizumab products in glioblastoma is based on an improvement in objective response rate. There are no data demonstrating an improvement in disease-related symptoms or increased survival with bevacizumab products.

MVASI is indicated for the treatment of metastatic renal cell carcinoma with interferon alfa.

MVASI is indicated for the treatment of cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.

MVASI 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.

MVASI U.S. Important Safety Information

Boxed WARNINGS

Gastrointestinal (GI) Perforations

The incidence of gastrointestinal perforation, some fatal, in bevacizumab product-treated patients ranges from 0.3-3.2%. Fatal outcome was reported in <1% of bevacizumab-treated patients. Discontinue MVASI in patients with gastrointestinal perforation.

Surgery and Wound Healing Complications

The incidence of wound healing and surgical complications, including serious and fatal complications, is increased in bevacizumab product-treated patients. Discontinue MVASI in patients with wound dehiscence. The appropriate interval between termination of bevacizumab products and subsequent elective surgery required to reduce the risks of impaired wound healing/wound dehiscence has not been determined. Discontinue at least 28 days prior to elective surgery. Do not initiate MVASI for at least 28 days after surgery and until the surgical wound is fully healed.

Hemorrhage

Severe or fatal hemorrhage, including hemoptysis, gastrointestinal bleeding, central nervous system hemorrhage, epistaxis, and vaginal bleeding occur up to 5-fold more frequently in patients receiving bevacizumab products. Across indications, the incidence of grade ≥3 hemorrhagic events among patients receiving bevacizumab ranged from 0.4% to 6.9%. Do not administer MVASI to patients with serious hemorrhage or recent hemoptysis (≥1/2 tsp of red blood). Discontinue MVASI in patients with serious hemorrhage (ie, requiring medical intervention).

Additional serious adverse events

- Additional serious and sometimes fatal adverse events with increased incidence in the bevacizumab product-treated arm vs control included
    - GI fistulae (up to 2% in metastatic colorectal cancer)
    - Non-GI fistulae (<1% in trials across various indications; 1.8% in a cervical cancer trial)
    - Arterial thromboembolic events (grade ≥3, 2.6%)
    - Proteinuria (nephrotic syndrome, <1%)
- Additional serious adverse events with increased incidence in the bevacizumab product-treated arm vs control included
    - GI-vaginal fistulae occurred in 8.3% of patients in a cervical cancer trial
    - Venous thromboembolism (grade 3-4, up to 10.6%) in patients with persistent, recurrent, or metastatic cervical cancer treated with chemotherapy and bevacizumab product
    - Hypertension (grade 3-4, 5%-18%)

    - Posterior reversible encephalopathy syndrome (PRES) (<0.5%)
- Infusion reactions with the first dose of bevacizumab product-treated patients were uncommon (<3%), and severe reactions occurred in 0.2% of patients
- Inform females of reproductive potential of the risk of ovarian failure prior to starting treatment with MVASI

Pregnancy warning

- Based on the mechanism of action and animal studies, bevacizumab products may cause fetal harm
- Advise female patients that MVASI may cause fetal harm, and to inform their healthcare provider of a known or suspected pregnancy
- Advise females of reproductive potential to use effective contraception during treatment with MVASI and for 6 months after the last dose of MVASI
- Advise nursing women that breastfeeding is not recommended during treatment with MVASI
- MVASI may impair fertility

Most Common Adverse Events

- Across indications, the most common adverse reactions observed in bevacizumab product-treated patients at a rate of >10% and at least twice the control arm rate were: epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, rectal hemorrhage, lacrimation disorder, back pain, exfoliative dermatitis
- Across all studies, bevacizumab product was discontinued in 8.4% to 21% of patients because of adverse reactions.

Please see full Prescribing Information, including Boxed WARNINGS, at www.Amgen.com.

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 Biosimilars 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 more than 35 years of experience in biotechnology to create high quality biosimilars and reliably supply them to patients worldwide.

For more information, visit http://www.amgenbiosimilars.com and follow us on http://www.twitter.com/amgenbiosim.

About Amgen's Commitment to Oncology

Amgen Oncology is committed to helping patients take on some of the toughest cancers, such as those that have been resistant to drugs, those that progress rapidly through the body and those where limited treatment options exist. Amgen's supportive care treatments help patients combat certain side effects of strong chemotherapy, and our targeted medicines and immunotherapies focus on more than a dozen different malignancies, ranging from blood cancers to solid tumors. With decades of experience providing therapies for cancer patients, Amgen continues to grow its portfolio of innovative and biosimilar oncology medicines.

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 http://www.amgen.com and follow us on www.twitter.com/amgen.

About Allergan plc

Allergan plc (NYSE: AGN), headquartered in Dublin, Ireland, is a bold, global pharmaceutical company and a leader in a new industry model – Growth Pharma. Allergan is focused on developing, manufacturing and commercializing branded pharmaceuticals, devices and biologic products for patients around the world.

Allergan markets a portfolio of leading brands and best-in-class products for the central nervous system, eye care, medical aesthetics and dermatology, gastroenterology, women's health, urology and anti-infective therapeutic categories.

Allergan is an industry leader in Open Science, the Company's R&D model, which defines our approach to identifying and developing game-changing ideas and innovation for better patient care. This approach has led to Allergan building one of the broadest development pipelines in the pharmaceutical industry with 70+ mid-to-late stage pipeline programs in development.

Our Company's success is powered by our more than 16,000 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.

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 it 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 manufacturing 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. 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. Amgen may not be able to access the capital and credit markets on terms that are favorable to it, or at all. Amgen is increasingly dependent on information technology systems, infrastructure and data security. 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.

Allergan plc Forward-Looking Statements

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®, on our financial results; uncertainty associated with financial projections, projected cost reductions, 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, 2016 and Allergan's Quarterly Report on Form 10-Q for the period ended September 30, 2017. Except as expressly required by law, Allergan disclaims any intent or obligation to update these forward-looking statements.

Avastin® is registered trademark of Genentech.

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