Pfizer Receives U.S. FDA Approval for Its Oncology Biosimilar, ZIRABEV™ (bevacizumab-bvzr)

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Pfizer Inc. (NYSE:PFE) today announced the United States (U.S.) Food and Drug Administration(FDA) has approved ZIRABEV™ (bevacizumab-bvzr), a biosimilar to Avastin® (bevacizumab),1 for the treatment of five types of cancer: metastatic colorectal cancer; unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC); recurrent glioblastoma; metastatic renal cell carcinoma (RCC); and persistent, recurrent or metastatic cervical cancer.2

“Biosimilars like ZIRABEV can help increase access to impactful therapies, driving market competition that may ultimately lower costs and help address the diverse needs of patients living with cancer,” said Andy Schmeltz, Global President, Pfizer Oncology. “We are proud to add ZIRABEV to our growing oncology portfolio for U.S. patients living with a wide variety of tumor types.”

The FDA approval was based on review of a comprehensive data package which demonstrated biosimilarity of ZIRABEV to the reference product. This includes results from the REFLECTIONS B7391003 clinical comparative study, which showed clinical equivalence and found no clinically meaningful differences between ZIRABEV and the reference product in patients with advanced non-squamous NSCLC.3

“ZIRABEV represents a welcome addition to the treatment armamentarium in its approved indications, potentially providing physicians with a medicine that has a similar safety profile and efficacy as the reference product,” said Dr. Niels Reinmuth, Department of Thoracic Oncology, Asklepios Lung Clinic, Munich-Gauting, Germany and

lead author of the REFLECTIONS B7391003 study.4 “The FDA’s approval of ZIRABEV may provide an important new option for the treatment of multiple forms of cancer.”

Biosimilars have been a significant catalyst for change for the healthcare industry over the last decade, with the potential to create a more sustainable healthcare system. With more than 10 years of global in-market experience and six approved biosimilar products in the U.S., Pfizer is proud to be a leader and at the forefront of this vital healthcare segment. ZIRABEV is Pfizer’s second oncology monoclonal antibody (mAb) biosimilar to be approved by the FDA, following the FDA approval of TRAZIMERA™ (trastuzumab-qyyp) in March 2019.5 ZIRABEV was also approved for use in the European Union (EU) in February 2019 for the treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent NSCLC, advanced and/or metastatic RCC and persistent, recurrent or metastatic carcinoma of the cervix.6

About ZIRABEV (bevacizumab-bvzr)

ZIRABEV is a mAb biosimilar of the reference product, Avastin, which works by inhibiting the formation of new blood cells (angiogenesis) by specifically recognizing and binding to vascular endothelial growth factor (VEGF) protein. As part of the REFLECTIONS clinical trial program, ZIRABEV has been studied in nearly 400 patients to date.3,7,8,9

ZIRABEV IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Gastrointestinal Perforations and Fistulae. Serious and sometimes fatal gastrointestinal perforation occurred at a higher incidence in patients receiving bevacizumab products compared to patients receiving chemotherapy. Non-GI fistulae (<1% to 1.8%, highest in patients with cervical cancer). Discontinue for gastrointestinal perforations, tracheoesophageal fistula, grade 4 fistula, or fistula formation involving any internal organ Surgery and Wound Healing Complications. The incidence of wound healing and surgical complications, including serious and fatal complications, is increased in bevacizumab-treated patients. Withhold for at least 28 days prior to elective surgery. Do not administer for at least 28 days following surgery and until the wound is fully healed. Discontinue in patients who develop wound healing complications that require medical intervention or necrotizing fasciitis Hemorrhage. Severe or fatal hemorrhage, including hemoptysis, GI bleeding, hematemesis, central nervous system hemorrhage, epistaxis, and vaginal bleeding occurred up to 5-fold more frequently in patients receiving bevacizumab. In clinical studies, the incidence of grade ≥3 hemorrhagic events among

patients receiving bevacizumab ranged from 0.4% to 7%. Do not administer ZIRABEV to patients with serious hemorrhage or a recent history of hemoptysis (≥1/2 tsp of red blood). Discontinue ZIRABEV in patients who develop grade 3–4 hemorrhage Additional serious and sometimes fatal adverse events with increased incidence in the bevacizumab-treated arm vs chemotherapy arm included: Arterial thromboembolic events (grade ≥3, 5%, highest in patients with GBM). Discontinue in patients who develop a severe ATE. Renal injury and proteinuria. Monitor proteinuria during ZIRABEV therapy. Patients with a 2+ or greater urine dipstick reading should undergo 24-hour urine collection. Withhold for proteinuria >2 grams per 24 hours and resume when less than 2 grams per 24 hours. Discontinue in patients who develop nephrotic syndrome Grade 3–4 proteinuria ranged from 0.7% to 7% in clinical studies Nephrotic syndrome (<1%) Additional serious adverse events with increased incidence in the bevacizumab-treated arm vs chemotherapy arm included: Venous thromboembolism (grade ≥3, 11% seen in Study GOG-0240). Discontinue ZIRABEV in patients with a Grade 4 VTE, including pulmonary embolism Hypertension (grade 3–4, 5%–18%). Monitor blood pressure during treatment and, for ZIRABEV associated hypertension, continue monitoring after discontinuation. Withhold for severe hypertension. Discontinue for hypertensive crisis or hypertensive encephalopathy Posterior reversible encephalopathy syndrome (PRES) (<0.5%). Discontinue ZIRABEV in patients who develop PRES. Symptoms usually resolve or improve within days after discontinuing bevacizumab products, although some patients have experienced ongoing neurologic sequelae. Congestive heart failure (CHF) (1%). Discontinue ZIRABEV in patients who develop CHF Infusion-related reactions with the first dose of bevacizumab occurred in <3% of patients, and severe reactions occurred in 0.2% of patients. Decrease the rate of infusion for mild infusion-related reactions. Interrupt the infusion in patients with clinically significant infusion-related reactions and consider resuming at a slower rate following resolution. Discontinue in patients who develop a severe infusion-related reaction and administer appropriate medical therapy Inform females of reproductive potential of the risk of ovarian failure prior to initiating treatment with ZIRABEV

Pregnancy Warning

Based on the mechanism of action and animal studies, bevacizumab products may cause fetal harm Advise female patients that bevacizumab products 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 ZIRABEV and for 6 months after the last dose of ZIRABEV Advise nursing women that breastfeeding is not recommended during treatment with ZIRABEV and for 6 months following their last dose of treatment Bevacizumab products may impair fertility

Most Common Adverse Events

Across studies, the most common adverse reactions observed in bevacizumab patients at a rate >10% were: Epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, rectal hemorrhage, lacrimation disorder, back pain, exfoliative dermatitis Across all studies, bevacizumab was discontinued in 8% to 22% of patients because of adverse reactions
Indication-Specific Adverse Events

In first-line metastatic colorectal cancer (MCRC), the most common grade 3–4 events in Study 2107, which occurred at a (≥2%) higher incidence in the bevacizumab plus IFL vs IFL groups, were asthenia (10% vs 7%), abdominal pain (8% vs 5%), pain (8% vs 5%), hypertension (12% vs 2%), deep vein thrombosis (9% vs 5%), intra-abdominal thrombosis (3% vs 1%), syncope (3% vs 1%), diarrhea (34% vs 25%), constipation (4% vs 2%), leukopenia (37% vs 31%), and neutropenia (21% vs 14%) In second-line MCRC, the most common grade 3–5 (nonhematologic) and 4–5 (hematologic) events in Study E3200, which occurred at a higher incidence (≥2%) in the bevacizumab plus FOLFOX4 vs FOLFOX4 groups, were fatigue (19% vs 13%), diarrhea (18% vs 13%), sensory neuropathy (17% vs 9%), nausea (12% vs 5%), vomiting (11% vs 4%), dehydration (10% vs 5%), hypertension (9% vs 2%), abdominal pain (8% vs 5%), hemorrhage (5% vs 1%), other neurological (5% vs 3%), ileus (4% vs 1%), and headache (3% vs 0%). These data are likely to underestimate the true adverse event rates due to the reporting mechanisms used in this study In non–small cell lung cancer (NSCLC), grade 3–5 (nonhematologic) and grade 4–5 (hematologic) adverse events in Study E4599 occurring at a (≥2%) higher incidence in bevacizumab-treated patients vs controls were neutropenia (27% vs 17%), fatigue (16% vs 13%), hypertension (8% vs 0.7%), infection without neutropenia (7% vs 3%), venous thromboembolism (5% vs 3%), febrile neutropenia (5% vs 2%), pneumonitis/pulmonary infiltrates (5% vs 3%), infection with grade 3 or 4 neutropenia (4% vs 2%), hyponatremia (4% vs 1%), headache (3% vs 1%), and proteinuria (3% vs 0%) In recurrent glioblastoma (rGBM) Study EORTC 26101, 22% of patients discontinued treatment in the bevacizumab with lomustine arm due to adverse reactions compared with 10% of patients in the lomustine arm. In patients receiving bevacizumab with lomustine, the adverse reaction profile was similar to that observed in other approved indications In metastatic renal cell carcinoma (mRCC), the most common grade 3–5 adverse events in Study BO17705, occurring at a (≥2%) higher incidence in bevacizumab-treated patients vs controls, were fatigue (13% vs 8%), asthenia (10% vs 7%), proteinuria (7% vs 0%), hypertension (6% vs 1%, including hypertension and hypertensive crisis), and hemorrhage (3% vs 0.3%, including epistaxis, small intestinal hemorrhage, aneurysm ruptured, gastric ulcer hemorrhage, gingival bleeding,

hemoptysis, hemorrhage intracranial, large intestinal hemorrhage, respiratory tract hemorrhage, and traumatic hematoma) In persistent, recurrent, or metastatic cervical cancer, grade 3 or 4 adverse reactions in Study GOG-0240, occurring at a higher incidence (≥2%) in 218 patients receiving bevacizumab plus chemotherapy compared to 222 patients receiving chemotherapy alone, were abdominal pain (12% vs 10%), diarrhea (6% vs 3%), anal fistula (4% vs 0%), proctalgia (3% vs 0%), urinary tract infection (8% vs 6%), cellulitis (3% vs 0.5%), fatigue (14% vs 10%), hypertension (11% vs 0.5%), thrombosis (8% vs 3%), hypokalemia (7% vs 4%), hyponatremia (4% vs 1%), dehydration (4% vs 0.5%), neutropenia (8% vs 4%), lymphopenia (6% vs 3%), back pain (6% vs 3%), and pelvic pain (6% vs 1%)

INDICATIONS

Metastatic Colorectal Cancer

ZIRABEV, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer (mCRC).

ZIRABEV, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with mCRC who have progressed on a first-line bevacizumab product-containing regimen.

Limitation of Use: ZIRABEV is not indicated for adjuvant treatment of colon cancer.

First-Line Non-Squamous Non-Small Cell Lung Cancer

ZIRABEV, in combination with carboplatin and paclitaxel, is indicated for the first line treatment of patients with unresectable, locally advanced, recurrent or metastatic non–squamous non–small cell lung cancer (NSCLC).

Recurrent Glioblastoma

ZIRABEV is indicated for the treatment of recurrent glioblastoma (GBM) in adults.

Metastatic Renal Cell Carcinoma

ZIRABEV, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma (mRCC).

Persistent, Recurrent, or Metastatic Cervical Cancer

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

Please see full Prescribing Information for ZIRABEV (bevacizumab-bvzr).

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 18 approved innovative cancer medicines and biosimilars across more than 20 indications, including breast, prostate, kidney, lung and hematology. Pfizer Oncology is striving to change the trajectory of cancer.

Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of June 28, 2019. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about ZIRABEV (bevacizumab-bvzr), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the launch timing and commercial success of ZIRABEV in the United States; the

uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when applications for ZIRABEV may be filed in any other jurisdictions; whether and when any such other applications for ZIRABEV that may be pending or filed may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether ZIRABEV will be commercially successful; intellectual property and/or litigation implications; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of ZIRABEV; uncertainties regarding access challenges for our biosimilar products where our product may not receive appropriate formulary access or remains in a disadvantaged position relative to the innovator product; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

_____ 1 Avastinis a registered trademark of Genentech Inc. 2 ZIRABEV™ (bevacizumab-bvzr) Prescribing Information. New York. NY: Pfizer Inc: 2019. Available at http://labeling.pfizer.com/ShowLabeling.aspx?id=11860. 3 Socinski MA, Von Pawel J, Kasahara K, et al. A comparative clinical study of PF-06439535, a candidate bevacizumab biosimilar, and reference bevacizumab, in patients with advanced nonsquamous non-small cell lung cancer. Abstract 109. Presented at ASCO 2018. 4 American Cancer Society. Cancer Facts & Figures 2019. Available at https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf. Accessed June 2019. 5 TRAZIMERA™ (trastuzumab-qyyp) Prescribing Information. New York. NY: Pfizer Inc: 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761081s000lbl.pdf. Accessed

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