



U.S. FDA and European Medicines Agency Accept Regulatory Submissions for BOSULIF® (bosutinib) for the Treatment of Patients with Newly Diagnosed Ph+ Chronic Myeloid Leukemia

Tuesday, August 29, 2017 - 03:00am

Applications seek to expand approved use of BOSULIF into first- line treatment based on positive results from Phase 3 head-to-head trial

Pfizer Inc. (NYSE:PFE) and Avillion LLP today announced that a supplemental New Drug Application (sNDA) for BOSULIF® (bosutinib) has been accepted for filing and granted Priority Review by the U.S. Food and Drug Administration (FDA). If approved, the sNDA would expand the approved use of BOSULIF to include patients with newly diagnosed chronic phase Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML). BOSULIF is currently indicated in the U.S. for the treatment of adult patients with Ph+ CML with resistance or intolerance to prior therapy. Priority Review status accelerates FDA review time from 10 months to a goal of six months from the day of acceptance of filing, and is given to drugs that may offer major advances in treatment or may provide a treatment for which no adequate therapy exists. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is in December 2017.

In addition, the European Medicines Agency (EMA) has validated for review a Type II Variation application for use of BOSULIF in the same patient population. In Europe,

BOSULIF has conditional marketing authorization for the treatment of adult patients with Ph+ CML previously treated with one or more tyrosine kinase inhibitors (TKIs) and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options.

The submissions are based on results from BFORE (Bosutinib trial in First line chrOnic myelogenous leukemia tREatment), a multi-center, multinational, open-label Phase 3 study which showed BOSULIF 400 mg was associated with a significantly higher rate of patients achieving major molecular response (MMR) at 12 months (the primary endpoint) compared to the rate achieved in patients treated with imatinib. Results from the trial were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in May 2017 and at the European Hematology Association (EHA) Meeting in June 2017. The adverse events seen in the trial were consistent with the known safety profile for BOSULIF. The proposed dosing for the newly diagnosed patients is 400 mg daily, which is different from the currently approved dosing in patients who are resistant or intolerant to prior TKI therapy (500 mg daily).

“As physicians gained experience with BOSULIF, they have come to appreciate its favorable risk-benefit profile in patients with Ph-positive CML who no longer responded to or could not tolerate prior TKI therapy,” said Mace Rothenberg, MD, Chief Development Officer, Oncology, Pfizer Global Product Development. “At the 400 mg dose, we believe that the BFORE study demonstrates a similarly favorable risk-benefit in previously untreated patients with Ph-positive CML. We look forward to working with the FDA in our efforts to expand the label for BOSULIF to include this important group of patients.”

“These are important milestones for the CML community and for our partnership with Pfizer, which represent the commitment of both of our companies to work collaboratively toward our ultimate goal of improving the lives of patients,” said Allison Jaynes-Ellis, MD, Chief Executive Officer of Avillion.

Pfizer and Avillion entered into an exclusive collaborative development agreement in 2014 to conduct the BFORE trial. Under the terms of the agreement, Avillion provided funding and conducted the trial to generate the clinical data used to support these applications and other potential regulatory filings for marketing authorization for BOSULIF as first-line treatment for patients with chronic phase Ph+ CML. If approved for this indication, Avillion will be eligible to receive milestone payments from Pfizer. Pfizer retains all rights to commercialize BOSULIF globally.

Pfizer is advancing a broad range of therapies that leverage select pathways and mechanisms of action to address acute and chronic leukemias, myeloproliferative

disorders and lymphoma.

ABOUT CHRONIC MYELOID LEUKEMIA (CML)

Chronic myeloid leukemia (CML) is a rare blood cancer, which begins in the bone marrow, but often moves into the blood.¹ Researchers estimate that by 2020, more than 412,000 people worldwide will be diagnosed with leukemia (all types).² CML accounts for 10-15% of all incident leukemia cases.^{1,3} In the U.S., approximately 48,000 people are living with CML.⁴ Around 9,000 new CML cases will be diagnosed in the U.S. in 2017.⁵

ABOUT BOSULIF® (bosutinib)

BOSULIF® (bosutinib) is an oral, once-daily, tyrosine kinase inhibitor (TKI), which inhibits the Bcr-Abl kinase that promotes CML; it is also an inhibitor of Src-family kinases. BOSULIF was approved in September 2012 in the U.S. for the treatment of adult patients with Ph+ CML with resistance or intolerance to prior therapy and offers an important treatment option for these patients. In Europe, BOSULIF was granted conditional marketing authorization in March 2013 for the treatment of adult patients with Ph+ CML previously treated with one or more TKIs and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options. The current approved dose of BOSULIF is 500 mg orally once daily with food. For more information on BOSULIF resources available for healthcare professionals and patients, please visit www.BOSULIF.com.

IMPORTANT BOSULIF® (bosutinib) SAFETY INFORMATION

Contraindication: History of hypersensitivity to BOSULIF. Reactions have included anaphylaxis. Anaphylactic shock occurred in less than 0.2% of treated patients in clinical trials.

Gastrointestinal Toxicity: Diarrhea, nausea, vomiting, and abdominal pain can occur. In the clinical trial, median time to onset for diarrhea was 2 days, median duration was 2 days, and median number of episodes per patient was 3 (range 1-268). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Myelosuppression: Thrombocytopenia, anemia, and neutropenia can occur. Perform complete blood counts weekly for the first month and then monthly or as clinically indicated. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Hepatic Toxicity: Twenty percent of patients experienced an increase in either ALT or AST. Liver enzyme elevation usually occurs early in treatment. The median time to onset

of increased ALT and AST was 35 and 33 days, respectively, and the median duration for each was 21 days. Perform hepatic enzyme tests at least monthly for the first 3 months and as clinically indicated. In patients with transaminase elevations, monitor liver enzymes more frequently. One case consistent with drug-induced liver injury occurred in a trial of BOSULIF in combination with letrozole. Withhold, dose reduce, or discontinue BOSULIF as necessary. In patients with mild, moderate, or severe hepatic impairment, the recommended starting dose is 200 mg daily.

Renal Toxicity: An on-treatment decline in estimated glomerular filtration rate has occurred in patients treated with BOSULIF. Monitor renal function at baseline and during therapy, with particular attention to patients with preexisting renal impairment or risk factors for renal dysfunction. Consider dose adjustment in patients with baseline and treatment emergent renal impairment. The recommended starting doses for patients with severe renal impairment (CrCL <30 mL/min) or moderate renal impairment (CrCL 30-50 mL/min) are 300 mg and 400 mg daily, respectively.

Fluid Retention: Fluid retention can occur and may cause pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. In the clinical trial, Grade 3/4 fluid retention was reported in 26 patients (5%). Monitor and manage patients using standards of care. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

Embryofetal Toxicity: BOSULIF can cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised of potential hazard to the fetus. Advise females of reproductive potential to use effective contraceptive measures to prevent pregnancy while being treated with BOSULIF and for at least 30 days after the final dose.

Adverse Reactions: The most common adverse reactions observed in greater than or equal to 20% of patients in the Phase 1/2 safety population (N=546) were diarrhea, nausea, thrombocytopenia, rash, vomiting, abdominal pain, respiratory tract infection, anemia, pyrexia, liver test abnormalities, fatigue, cough, and headache. The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of patients were thrombocytopenia, neutropenia, and anemia.

CYP3A Inhibitors and Inducers: Avoid concurrent use with strong or moderate CYP3A inhibitors or inducers.

Proton Pump Inhibitors: Consider using short-acting antacids or H₂ blockers instead of PPIs to avoid a reduction in BOSULIF exposure. Separate antacid or H₂ blocker dosing and BOSULIF dosing by more than 2 hours.

Nursing Mothers: Given the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or BOSULIF, taking into account the importance of the drug to the mother.

Please see full Prescribing Information at www.bosulif.com.

About Pfizer Oncology

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on those living with cancer. As a leader in oncology speeding cures and accessible breakthrough medicines to patients, Pfizer Oncology is helping to redefine life with cancer. Our strong pipeline of biologics, small molecules and immunotherapies, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments and licensing partners, Pfizer Oncology strives to cure or control cancer with its breakthrough medicines. Because Pfizer Oncology knows that success in oncology is not measured solely by the medicines you manufacture, but rather by the meaningful partnerships you make to have a more positive impact on people's lives.

Pfizer Inc.: 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 healthcare products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer healthcare 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 for investors to 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](https://www.facebook.com/Pfizer).

About Avillion

Avillion LLP is a drug development company with an innovative business model focusing on the clinical co-development and regulatory approval of late stage pharmaceutical products. Avillion offers a compelling opportunity to partner late-stage therapeutic projects for approval in the US and EU and to accelerate their availability to the market. Our objective is to enable our partners to continue to develop the drug candidates in their pipeline at the highest quality without increasing the burden on their P&L or cash reserves. Avillion can achieve this by incurring 100% of the clinical and regulatory risk, while advancing the development of these late-stage assets in return for milestone payments on the commercialisation of successfully developed products.

Avillion was founded in 2012 in London, UK, and is backed by Abingworth, Clarus Ventures and Royalty Pharma. <http://www.avillionllp.com>

PFIZER DISCLOSURE NOTICE: The information contained in this release is as of August 29, 2017. 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 a potential new indication for BOSULIF (bosutinib), 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, the uncertainties inherent in research and development, including the ability to meet anticipated trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; uncertainties regarding the commercial success of BOSULIF; whether and when any applications for the potential indication may be filed with regulatory authorities in any other jurisdictions; whether and when the FDA and EMA will approve the sNDA and Type II Variation application, respectively, for the potential indication and whether and when regulatory authorities in any jurisdictions may approve any such other applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of BOSULIF, including the potential indication; 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, 2016 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 American Cancer Society. What is Chronic Myeloid Leukemia?

<http://www.cancer.org/acs/groups/cid/documents/webcontent/003112-pdf.pdf>. Accessed August 2017.

2 GLOBOCAN Online Analysis/Prediction.

http://globocan.iarc.fr/old/burden.asp?selection_pop=224900&Text-p=World&selection_cancer=12280&Text-c=Leukaemia&pYear=8&type=0&window=1&submit=%C2%A0Execute. Accessed August 2017.

3 Hochhaus, A. Educational Session: Managing Chronic Myeloid Leukemia as a Chronic Disease. American Society of Hematology. 2011; 10: 1.

4 National Cancer Institute. Surveillance Epidemiology and End Results (SEER) Statistics Stratified by Cancer Site: Chronic Myeloid Leukemia Prevalence.

<http://seer.cancer.gov/faststats/selections.php?run=runit&output=2&data=5&statistic=9&race=> Accessed August 2017.

5 American Cancer Society. What Are the Key Statistics About Chronic Myeloid Leukemia?

<https://www.cancer.org/cancer/chronic-myeloid-leukemia/about/statistics.html>. Accessed August 2017.

Pfizer Media: Sally Beatty, 212-733-6566 or Pfizer Investors: Ryan Crowe, 212-733-8160 or Avillion: Allison Jeynes-Ellis, +44 (0)203 764 9531 or Avillion Media: Citigate Dewe Rogerson Mark Swallow, +44 (0)207 282 2948