



NEWS RELEASE

IMBRUVICA® (ibrutinib) Supplemental New Drug Application for Treatment-naïve Chronic Lymphocytic Leukemia Submitted to the U.S. FDA

9/14/2015

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Submission seeking potential fifth indication based on data from the Phase 3 RESONATE[®]-2 (PCYC-1115) trial HORSHAM, PA, September 14, 2015 - A supplemental New Drug Application (sNDA) for IMBRUVICA® (ibrutinib) has been submitted to the U.S. Food and Drug Administration (FDA) for front-line use in patients with chronic lymphocytic leukemia (CLL), Janssen Biotech Inc. announced today. The filing is based on data from the randomized, multi-center, open-label Phase 3 RESONATE[™]-2 (PCYC-1115) trial assessing the use of ibrutinib versus chlorambucil in patients with treatment-naïve CLL or small lymphocytic lymphoma (SLL) aged 65 years or older. IMBRUVICA is jointly developed and commercialized by Janssen and Pharmacyclics LLC, an AbbVie company. Pharmacyclics is the investigational new drug (IND) holder for IMBRUVICA in the U.S. and submitted the application to the FDA on behalf of the companies.

"Treatment-naïve patients with this disease typically relapse or become refractory to standard chemotherapy, so new options are greatly needed to potentially change the CLL/SLL treatment paradigm," said Jan Burger, M.D., Ph.D., Associate Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX and study lead investigator.

The RESONATE-2 trial enrolled 269 patients with treatment-naïve CLL/SLL aged 65 years or older in the U.S., EU and other regions. Patients were randomized to receive either ibrutinib 420 mg orally, once daily until progression or toxicity or chlorambucil 0.5 to 0.8 mg/kg on days 1 and 15 of each 28-day cycle for up to 12 cycles. At the time of the final analysis, the primary endpoint was met, with ibrutinib shown to be superior to chlorambucil in terms of

progression-free survival (PFS). In addition, ibrutinib demonstrated significant improvements in key secondary efficacy endpoints, including overall survival (OS), overall response rate (ORR) and in hematologic function.

"This submission to expand the use of IMBRUVICA for patients with treatment-naïve CLL is very significant, as this patient population represents the largest group of patients with CLL," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Head, Janssen Research & Development, LLC. "The submission highlights our commitment to developing medicines that truly transform treatment paradigms and patient outcomes, as well as our commitment to further develop IMBRUVICA in hematologic malignancies."

The RESONATE-2 trial was sponsored by Pharmacyclics. The data have been submitted for presentation at an upcoming medical conference and for publication in a peer-reviewed journal. More information about the study can be found on www.clinicaltrials.gov.

Janssen Research & Development, LLC and Pharmacyclics are continuing an extensive clinical development program for IMBRUVICA, including Phase 3 study commitments in multiple patient populations.

About CLL CLL is a slow-growing blood cancer that most commonly arises from B cells, a type of white blood cell (lymphocyte) that originates in the bone marrow.^{1,2} CLL is predominantly a disease of the elderly, with a median age of 71 at diagnosis.³

About IMBRUVICA® (ibrutinib) IMBRUVICA was one of the first therapies to receive U.S. approval after having received the FDA's Breakthrough Therapy Designation. IMBRUVICA works by blocking a specific protein called Bruton's tyrosine kinase (BTK).¹ The BTK protein transmits important signals that tell B cells to mature and produce antibodies and is needed by specific cancer cells to multiply and spread.^{1,4} IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.¹ For more information, visit www.IMBRUVICA.com.

Additional Information about IMBRUVICA®

INDICATIONS

IMBRUVICA® is indicated to treat people with:

- Chronic lymphocytic leukemia (CLL) who have received at least one prior therapy
- Chronic lymphocytic leukemia (CLL) with 17p deletion
- Waldenström's macroglobulinemia (WM)
- Mantle cell lymphoma (MCL) who have received at least one prior therapy
 - Accelerated approval was granted for this indication based on overall response rate. Continued

approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA[®]. Grade 3 or higher bleeding events (subdural hematoma, gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half of patients treated with IMBRUVICA[®].

The mechanism for the bleeding events is not well understood. IMBRUVICA[®] may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies. Consider the benefit-risk of withholding IMBRUVICA[®] for at least 3 to 7 days pre and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections - Fatal and non-fatal infections have occurred with IMBRUVICA[®] therapy. Grade 3 or greater infections occurred in 14% to 26% of patients. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA[®]. Monitor patients for fever and infections and evaluate promptly.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 19 to 29%), thrombocytopenia (range, 5 to 17%), and anemia (range, 0 to 9%) occurred in patients treated with IMBRUVICA[®]. Monitor complete blood counts monthly.

Atrial Fibrillation - Atrial fibrillation and atrial flutter (range, 6 to 9%) have occurred in patients treated with IMBRUVICA[®], particularly in patients with cardiac risk factors, acute infections, and a previous history of atrial fibrillation. Periodically monitor patients clinically for atrial fibrillation. Patients who develop arrhythmic symptoms (e.g., palpitations, lightheadedness) or new-onset dyspnea should have an ECG performed. If atrial fibrillation persists, consider the risks and benefits of IMBRUVICA[®] treatment and dose modification.

Second Primary Malignancies - Other malignancies (range, 5 to 14%) including non-skin carcinomas (range, 1 to 3%) have occurred in patients treated with IMBRUVICA[®]. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4 to 11%).

Tumor Lysis Syndrome - Tumor lysis syndrome has been reported with IMBRUVICA[®] therapy. Monitor patients closely and take appropriate precautions in patients at risk for tumor lysis syndrome (e.g., high tumor burden).

Embryo-Fetal Toxicity - Based on findings in animals, IMBRUVICA[®] can cause fetal harm when administered to a pregnant woman. Advise women to avoid becoming pregnant while taking IMBRUVICA[®]. If this drug is used during

pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

ADVERSE REACTIONS The most common adverse reactions ($\geq 25\%$) in patients with B-cell malignancies (MCL, CLL, WM) were thrombocytopenia* (57%, 52%, 43%), neutropenia* (47%, 51%, 44%), diarrhea (51%, 48%, 37%), anemia* (41%, 36%, 13%), fatigue (41%, 28%, 21%), musculoskeletal pain (37%, 28%†, NA‡), bruising (30%, 12%†, 16%†), nausea (31%, 26%, 21%), upper respiratory tract infection (34%, 16%, 19%), and rash (25%, 24%†, 22%†).

*Based on adverse reactions and/or laboratory measurements (noted as platelets, neutrophils, or hemoglobin decreased).

†Includes multiple ADR terms.

‡Not applicable; no associated ADRs.

The most common Grade 3 or 4 non-hematological adverse reactions ($\geq 5\%$) in MCL patients were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), diarrhea (5%), fatigue (5%), and skin infections (5%). Approximately 6% (CLL), 14% (MCL), and 11% (WM) of patients had a dose reduction due to adverse events. Approximately 5% (CLL), 9% (MCL), and 6% (WM) of patients discontinued due to adverse events. Most frequent adverse events leading to discontinuation were infections, subdural hematomas, and diarrhea in CLL patients and subdural hematoma (1.8%) in MCL patients.

DRUG INTERACTIONS

CYP3A Inhibitors - Avoid co-administration with strong and moderate CYP3A inhibitors. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA[®] dose.

CYP3A Inducers - Avoid co-administration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment - Avoid use in patients with moderate or severe baseline hepatic impairment. In patients with mild impairment, reduce IMBRUVICA[®] dose.

Please see full Prescribing Information:

http://www.imbruvica.com/downloads/Prescribing_Information.pdf

About Janssen Biotech, Inc. Janssen Biotech, Inc. redefines the standard of care in immunology, oncology, urology and nephrology. Built upon a rich legacy of innovative firsts, Janssen Biotech has delivered on the promise of new treatments and ways to improve the health of individuals with serious disease. Beyond its innovative medicines, Janssen Biotech is at the forefront of developing education and public policy initiatives to ensure patients and their families, caregivers, advocates and health care professionals have access to the latest treatment information, support services and quality care.

Janssen Biotech, Inc. and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. For more information on Janssen Biotech, Inc. or its products, visit <http://www.janssenbiotech.com>. Follow us on Twitter at www.twitter.com/JanssenUS.

Janssen in Oncology In oncology, our goal is to fundamentally alter the way cancer is understood, diagnosed and managed, reinforcing our commitment to the patients who inspire us. In looking to find innovative ways to address the cancer challenge, our primary efforts focus on several treatment and prevention solutions. These include a focus on hematologic malignancies, prostate cancer and lung cancer; cancer interception with the goal of developing products that interrupt the carcinogenic process; biomarkers that may help guide targeted, individualized use of our therapies; as well as safe and effective identification and treatment of early changes in the tumor microenvironment. Please visit oncology.janssenrnd.com.

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Cautions Concerning Forward-Looking Statements This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Biotech, Inc., Janssen Research & Development, LLC and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in new product development, including the uncertainty of clinical success and of obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 28, 2014, including in Exhibit 99 thereto, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

References:

¹ American Cancer Society. Detailed guide: what is chronic lymphocytic leukemia. Available from: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003111-pdf.pdf> Accessed September 2015. ² Shaffer AL, Rosenwald A, Staudt LM. Lymphoid malignancies: the dark side of B-cell differentiation. *Nat Rev Immunol.* 2002;2(12):920-932. ³ American Cancer Society. What are the key statistics for chronic lymphocytic leukemia? Available from: <http://www.cancer.org/cancer/leukemia-chroniclymphocyticcll/detailedguide/leukemia-chronic-lymphocytic-key-statistics>. Accessed: September 2015 ⁴ Genetics Home Reference. Isolated growth hormone deficiency. Available from: <http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency>. Accessed September 2015.

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