NEWS RELEASE

U.S. FDA Approves IMBRUVICA® (ibrutinib) for the Treatment of Waldenström's Macroglobulinemia: First FDA-Approved Therapy for This Disease

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HORSHAM, PA, January 29, 2015 - Janssen Biotech, Inc. ("Janssen") today announced that the U.S. Food and Drug Administration (FDA) has approved IMBRUVICA® (ibrutinib) capsules as the first therapy indicated specifically for patients with Waldenström's macroglobulinemia (WM),[1] a rare, indolent type of B-cell lymphoma. This represents the fourth indication for IMBRUVICA since its initial approval in **November 2013**. IMBRUVICA was granted **Breakthrough Therapy Designation** for WM by the FDA and is being jointly developed and commercialized by Janssen and Pharmacyclics, Inc.

The update to the IMBRUVICA label is based on data from a Dana-Farber Cancer Institute Phase 2 study. Earlier releases of these data were previously presented at the 2013 American Society of Hematology (ASH) and the 2013 International Congress of Malignant Lymphoma (ICML) annual meetings.

"Since the first description of Waldenström's macroglobulinemia more than 70 years ago, there has been no approved treatment for this cancer. Rather, doctors relied on therapies borrowed from similar cancers to treat these patients. I am truly grateful to the FDA for their thorough review and expedited approval of IMBRUVICA for this indication. The approval was made possible because of the hard work and dedication of scientists and clinicians at various leading medical centers who diligently worked on the clinical trial that supports IMBRUVICA as a safe and effective therapy for patients with Waldenström's macroglobulinemia," said Steven P. Treon, M.D., Ph.D., Director of the Bing Center for Waldenström's Macroglobulinemia at the Dana-Farber Cancer Institute and Associate Professor at Harvard Medical School, and, who led the trial.

"Waldenström's macroglobulinemia patients and physicians have been waiting for a treatment specifically studied and approved to treat this rare disease," said Carl Harrington, President of the International Waldenstrom's Macroglobulinemia Foundation. "The approval of IMBRUVICA is an important milestone for the entire global WM community and has the potential to positively impact our patients, their physicians and caregivers."

The Phase 2 multi-center study on which this approval was based evaluated the efficacy and tolerability of IMBRUVICA 420 mg once daily in 63 patients with previously treated WM (median age of 63; range, 44-86 years old). The response rate as assessed by an Independent Review Committee using criteria adopted from the International Workshop on WM was 62 percent (95% CI, 48.8, 73.9). Nearly 51 percent of patients achieved a partial response (PR) and 11 percent achieved a very good PR. No complete responses were reported. The median duration of response has not been reached (2.8+, 18.8+ months). The median time to response was 1.2 months (range, 0.7-13.4 months).

The most commonly occurring adverse reactions in the WM trial (≥20 percent of IMBRUVICA patients) were neutropenia (decreased amount of neutrophils in the blood), thrombocytopenia (decrease in platelets in the blood), diarrhea, rash, nausea, muscle spasms and fatigue. Six percent of patients in the WM trial receiving IMBRUVICA discontinued treatment due to adverse events. Adverse events leading to dose reduction occurred in 11 percent of patients.

"The IMBRUVICA Waldenström's macroglobulinemia approval is a sterling example of collaboration for the benefit of patients," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Head, Janssen. "All partners involved recognized the urgent need for approved treatment options for those living with WM, and collectively set an aggressive pace to gain approval. The fact that the FDA granted full approval for this indication is meaningful and confirms the safety and efficacy of IMBRUVICA in WM."

In the U.S., there are approximately 1,000 to 1,500 new cases of WM each year and the median age at diagnosis is 60 to 70 years of age.[2,3] WM (a clinically recognized subset of lymphoplasmacytic lymphoma, or LPL) begins with a malignant change to the B cell, a type of white blood cell (lymphocyte), during its maturation so that it continues to reproduce more malignant B cells.[4] WM cells make large amounts of a certain type of antibody (immunoglobulin M, or IgM) mostly in the bone marrow.[4] Antibodies such as IgM normally help the body to fight infection.[4] However, the overproduction of IgM, a hallmark of WM, often leads to the bone marrow becoming dysfunctional.[4] Typically, patients with WM are diagnosed after developing symptoms associated with the disease such as anemia, fatigue and night sweats.[4]

About IMBRUVICA

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,] IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.[1] For more information, visit **www.IMBRUVICA.com**.

Janssen and Pharmacyclics are striving to make the process of obtaining IMBRUVICA and navigating insurance benefits easy for patients. The YOU&i™ Support Program is a personalized program that includes information on access and affordability, nurse call support and resources for patients being treated with IMBRUVICA. This includes the YOU&i™ Instant Savings program, which provides co-pay support and benefits information to eligible commercially-insured patients. This program is not valid for patients with Medicare or Medicaid. Patients can access the program by contacting 1-877-877-3536, option 1 or by visiting **http://www.imbruvica.com**.

Additional Information about IMBRUVICA®
INDICATIONS
IMBRUVICA is indicated to treat people with:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy
    - o 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.
- Chronic lymphocytic leukemia (CLL) who have received at least one prior therapy
- Chronic lymphocytic leukemia (CLL) with 17p deletion
- Waldenström's macroglobulinemia (WM)

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 (eg, 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 (≥25%) in patients with B-cell malignancies (MCL, CLL, WM) were thrombocytopenia, neutropenia, diarrhea, anemia, fatigue, musculoskeletal pain, bruising, nausea, upper respiratory tract infection, and rash. Seven percent of patients receiving IMBRUVICA® discontinued treatment due to adverse events.

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. For more information on Janssen Biotech, Inc. or its products, visit **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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[1] IMBRUVICA Prescribing Information, January 2015.

[2] American Cancer Society. "What are the key statistics about Waldenstrom macroglobulinemia?" Available at: **http://www.cancer.org/cancer/waldenstrommacroglobulinemia/detailedguide/waldenstrom-macroglobulinemia-key-statistics-w-m**. Accessed January 2015.

[3] Fonseca R, Hayman S. Waldenström macroglobulinaemia. Br J Haematol. 2007;138(6)700-720.

[4] American Cancer Society. "What is Waldenstrom macroglobulinemia?" Available at: **http://www.cancer.org/cancer/waldenstrommacroglobulinemia/detailedguide/waldenstrom-macroglobulinemia-w-m**. Accessed January 2015.

[5] Genetics Home Reference. Isolated growth hormone deficiency. Available at: **http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency**. Accessed January 2015.

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