NEWS RELEASE

U.S. FDA Approves IMBRUVICA® (ibrutinib) for First-line Treatment of Chronic Lymphocytic Leukemia

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HORSHAM, Pa., March 4, 2016 -The U.S. Food and Drug Administration (FDA) has approved IMBRUVICA® (ibrutinib) capsules for treatment-naïve patients with chronic lymphocytic leukemia (CLL).[1] The approval is based on data from the Phase 3 **RESONATE-2** (PCYC-1115) study, the first head-to-head clinical trial comparing IMBRUVICA to a chemotherapy agent. Results showed IMBRUVICA significantly extended progression-free survival (PFS; the primary endpoint) and increased overall response rate (ORR; a key secondary endpoint) compared to chlorambucil in previously untreated patients with CLL age 65 or older. IMBRUVICA is now approved for use in all lines of CLL therapy, considerably expanding the number of patients who may benefit from this treatment. This broadens the indication beyond the initial CLL approval in **February 2014** for the treatment of patients with CLL who have received at least one prior therapy and in **July 2014** for CLL patients with del 17p,[1] a genetic mutation typically associated with poor treatment outcomes.[2] IMBRUVICA is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.

On a related front, the National Comprehensive Cancer Network® (NCCN) published an update on February 17 to its **Clinical Practice Guidelines** for non-Hodgkin's lymphomas recommending IMBRUVICA for certain first-line CLL patients.

"People living with CLL who have not been previously treated now have an option that significantly improved progression-free survival when compared to the oral chemotherapy used in the RESONATE-2 trial," 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 RESONATE-2 study lead investigator. "The results seen in the RESONATE-2 clinical trial are truly compelling and make this medicine an attractive first-line treatment option for clinicians in

the hematology space."

The expanded IMBRUVICA indication is based on data from the Phase 3, randomized, open-label RESONATE-2 trial, which showed IMBRUVICA significantly improved PFS and ORR versus chlorambucil in treatment-naïve patients aged 65 or older with CLL or small lymphocytic lymphoma (SLL). The PFS as assessed by an Independent Review Committee (IRC) according to the clarified International Workshop on Chronic Lymphocytic Leukemia (iWCLL) criteria indicated an 84 percent statistically significant reduction in the risk of death or progression in the IMBRUVICA arm versus the chlorambucil arm (HR=0.161 [95 percent CI, 0.091-0.283]). Median PFS was not reached for IMBRUVICA versus 18.9 months for chlorambucil (95 percent CI: 14.1, 22.0). Data from **RESONATE-2** were presented in an oral session at the American Society of Hematology (ASH) Annual Meeting on December 7, 2015, in addition to being featured in the official ASH press program and simultaneously published online in **The New England Journal of Medicine**.

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.[3,4] CLL is predominantly a disease of the elderly, with a median age of 71 at diagnosis.[5]

"The IMBRUVICA story gets better and better. The results of RESONATE-2 demonstrate how IMBRUVICA can change the treatment strategies for many patients with CLL in the treatment-naïve setting. We anticipate this approval will give clinicians and more of their patients the opportunity to explore the efficacy and safety of treatment with IMBRUVICA for this disease," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Head, Janssen Research & Development, LLC.

Janssen and Pharmacyclics continue to support an extensive clinical development program for IMBRUVICA, including 16 Phase 3 study commitments in multiple patient populations.

IMBRUVICA in First-line, Elderly CLL Patients

The safety and efficacy of IMBRUVICA were evaluated in the randomized, international, multi-center, open-label Phase 3 RESONATE-2 trial in 269 treatment-naïve patients with CLL/SLL* aged 65 years or older. Patients were randomized to receive either IMBRUVICA 420 mg orally, once daily until progression or unacceptable 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, with an allowance for intrapatient dose increases up to 0.8mg/kg based on tolerability.

The primary endpoint of the study was met, with IMBRUVICA demonstrating a longer PFS versus chlorambucil as determined by the IRC per clarified iWCLL criteria. The hazard ratio was 0.161 (95 percent CI, 0.091-0.283, P<0.0001), which represents a reduction of risk of progression or death by 84 percent versus chlorambucil (median PFS not reached for IMBRUVICA vs. 18.9 months for chlorambucil [95 percent CI: 14.1, 22.0]); IMBRUVICA was

associated with a significantly higher ORR (a composite of complete and partial responses [82.4 percent vs. 35.3 percent; P<0.0001]) as assessed by the IRC per modified iWCLL criteria. Notably, five patients (3.7 percent) in the IMBRUVICA arm and two patients (1.5 percent) in the chlorambucil arm achieved a complete response.

The safety of IMBRUVICA in this patient population was consistent with previously reported studies. The adverse reactions (AR) reported in the U.S. Prescribing Information reflect exposure to IMBRUVICA with a median duration of 17.4 months versus a median exposure to chlorambucil of 7.1 months: nearly 2.5 times longer exposure for IMBRUVICA. Warnings and Precautions include hemorrhage, infections, cytopenias, atrial fibrillation, hypertension, second primary malignancies, tumor lysis syndrome and embryo-fetal toxicity. The most common ARs (≥20 percent) of any Grade in the RESONATE-2 trial for IMBRUVICA were diarrhea (42 percent), musculoskeletal pain** (36 percent), cough (22 percent) and rash** (21 percent). The most common Grade 3/4 AR (≥five percent) was pneumonia** (eight percent). Four to 10 percent of patients receiving IMBRUVICA in the studies supporting the CLL indications (PCYC-1102, RESONATE [PCYC-1112] and RESONATE-2) discontinued treatment due to ARs. These included pneumonia, subdural hematomas and atrial fibrillation (one percent each). ARs leading to dose reduction occurred in approximately four percent of patients.

*IMBRUVICA is not approved by the FDA to treat SLL.

**includes multiple ADR terms

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.[1,6] IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.[1] For more information, visit **www.IMBRUVICA.com**.

Access to IMBRUVICA

Janssen and AbbVie are striving to make access to IMBRUVICA easy by helping patients understand their insurance benefits for IMBRUVICA. The YOU&i&#8482 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&#8482 Instant Savings program, which provides co-pay support to eligible commercially insured IMBRUVICA 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 **www.IMBRUVICA.com** .

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (intracranial hemorrhage [including 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 and patients should be monitored for signs of bleeding. Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and postsurgery depending on the type of surgery and the risk of bleeding.

Infections - Fatal and nonfatal 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®. Evaluate patients for fever and infections and treat appropriately.

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, hypertension, 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. Atrial fibrillation should be managed appropriately and if it persists, consider the risks and benefits of IMBRUVICA® treatment and dose modification.

Hypertension - Hypertension (range, 6% to 17%) has occurred in patients treated with IMBRUVICA® with a median time to onset of 4.5 months (range, 0.03 to 18.40 months). Monitor patients for new-onset hypertension or hypertension that is not adequately controlled after starting IMBRUVICA®. Adjust existing antihypertensive medications and/or initiate antihypertensive treatment as appropriate.

Second Primary Malignancies - Other malignancies (range, 5% to 16%) including non-skin carcinomas (range, 1% to 4%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4% to 13%).

Tumor Lysis Syndrome - Tumor lysis syndrome has been infrequently reported with IMBRUVICA® therapy. Assess the baseline risk (eg, high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

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® and for 1 month after cessation of therapy. 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 (≥20%) in patients with B-cell malignancies (MCL, CLL, WM) were thrombocytopenia* (57%, 53%, 43%), diarrhea (51%, 48%, 37%), anemia* (41%, 37%, 13%), neutropenia* (47%, 46%, 44%), musculoskeletal pain (37%, 32%†, NA‡), fatigue (41%, 29%, 21%), bruising (30%, 25%†, 16%†), nausea (31%, 24%, 21%), rash (25%, 23%†, 22%†), and upper respiratory tract infection (34%, 19%, 19%).

*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-hematologic adverse reactions (≥5%) in MCL patients were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), diarrhea (5%), fatigue (5%), and skin infections (5%).

Approximately 4% (CLL), 14% (MCL), and 11% (WM) of patients had a dose reduction due to adverse reactions.

Approximately 4-10% (CLL), 9% (MCL), and 6% (WM) of patients discontinued due to adverse reactions. Most frequent adverse events leading to discontinuation were pneumonia, subdural hematomas, and atrial fibrillation (1% each) in CLL patients and subdural hematoma (1.8%) in MCL patients.

DRUG INTERACTIONS

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

CYP3A Inducers - Avoid coadministration 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.janssen.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 **www.janssen.com**.

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. 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 January 3, 2016, 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.

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[1] IMBRUVICA Prescribing Information, March 2016.

[2] NCCN Clinical Practice Guidelines in Oncology. Non-Hodgkin's Lymphomas. Version 2.2016. Available from: **http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf.** Accessed March 2016.

[3] 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 March 2016.

[4] Shaffer AL, Rosenwald A, Staudt LM. Lymphoid malignancies: the dark side of B-cell differentiation. Nat Rev Immunol. 2002;2(12):920-932.

[5] 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 March 2016.

[6] Genetics Home Reference. Isolated growth hormone deficiency. Available from: **http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency**. Accessed March 2016.

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