News Release

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U.S. FDA Approves IMBRUVICA® (ibrutinib) Plus Rituximab for the Treatment of Patients with Chronic Lymphocytic Leukemia (CLL)

Patients ages 70 years or younger who were new to CLL treatment lived longer without disease progression with the IMBRUVICA®-based regimen compared to patients treated with a chemoimmunotherapy regimen

HORSHAM, Pa., April 21, 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the U.S. Food and Drug Administration (FDA) approval of IMBRUVICA® (ibrutinib) in combination with rituximab for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who are new to therapy. The approval is based on positive results from the landmark Phase 3 E1912 study that was designed and conducted by the ECOG-

ACRIN Cancer Research Group (ECOG-ACRIN) and sponsored by the National Cancer Institute, part of the National Institutes of Health. Today's milestone marks the 11th U.S. FDA approval for IMBRUVICA® across six disease areas and is the sixth approval for IMBRUVICA® in CLL.

The E1912 study showed newly diagnosed patients ages 70 years or younger (median age of 58 years) treated with IMBRUVICA® plus rituximab lived longer without disease progression, with a progression-free survival (PFS) rate of 88 percent at 37 months, compared to patients treated with fludarabine, cyclophosphamide and rituximab (FCR), with a PFS rate of 75 percent. Extended follow-up results from the E1912 study were most recently presented at the 2019 American Society of Hematology (ASH) Annual Meeting.

"FCR, a chemoimmunotherapy-based regimen, has been the standard of care for many previously untreated younger patients with CLL. With the introduction of this ibrutinib-rituximab combination, patients now have a more effective, non-chemoimmunotherapy option," said Brian Koffman, M.D., C.M. (retired), Co-Founder and Chief Medical Officer/Executive Vice President, CLL Society, a nonprofit organization focused on CLL patient education, support and research. "In the 14 years since I was first diagnosed with CLL, the treatment landscape has advanced dramatically for the better, with ibrutinib continuing to play a pioneering role in defining what it means to live with this disease."

The IMBRUVICA® application received approval through the U.S. FDA's Real-Time Oncology Review (RTOR) pilot program and received Priority Review designation. Additionally, the approval was granted under a modified version of the newly established Project Orbis, an initiative of the FDA Oncology Center of Excellence, which provides a framework for submission and review of oncology medicine applications among international regulatory agencies.[1]

"We commend the ECOG-ACRIN Cancer Research Group and the National Cancer Institute for conducting a robust study that has generated insightful and landmark

results in the treatment of CLL," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "We are committed to the continued study of IMBRUVICA-based regimens and building upon the efficacy and safety of the most comprehensively studied BTK inhibitor in our efforts to improve the lives of patients facing a blood cancer diagnosis."

Warnings and Precautions include: hemorrhage, infections, cytopenias, cardiac arrhythmias, hypertension, second primary malignancies, tumor lysis syndrome, and embryo-fetal toxicity. In the E1912 study, the most common adverse reactions (occurring in 15 percent or more of patients) of all Grades in patients treated with IMBRUVICA® plus rituximab were fatigue (80 percent), musculoskeletal pain* (61 percent), diarrhea (53 percent), rash* (49 percent), hypertension* (42 percent), arthralgia (41 percent), nausea (40 percent), headache (40 percent), bruising* (36 percent), cough (32 percent), hemorrhage* (31 percent), upper respiratory tract infection (29 percent), peripheral edema (28 percent), pyrexia (27 percent), pain (23 percent), stomatitis* (22 percent), and dyspnea (22 percent).

The recommended dosage of IMBRUVICA® for CLL/SLL is 420 mg orally once a day until disease progression or unacceptable toxicity. For CLL/SLL, IMBRUVICA® can be administered as a single agent, in combination with rituximab or obinutuzumab, or in combination with bendamustine and rituximab (BR). When administering IMBRUVICA® in combination with rituximab or obinutuzumab, consider administering IMBRUVICA® prior to rituximab or obinutuzumab when given on the same day.

*Includes multiple adverse drug reaction terms.

About the E1912 Study

The study evaluated 529 previously untreated CLL patients ages 70 years or younger (median age of 58) who were randomly assigned to receive IMBRUVICA® plus rituximab (n=354) or the chemoimmunotherapy FCR (n=175). With a median

follow-up time on study of 37 months, PFS benefits were observed for the IMBRUVICA® plus rituximab arm as compared to the FCR treatment arm (hazard ratio [HR], 0.34; 95 percent confidence interval [CI], 0.22-0.52; p<0.0001). With a median follow-up time of 49 months, median overall survival was not reached with a total of 23 deaths: 11 (3 percent) in the IMBRUVICA® plus rituximab and 12 (7 percent) in the FCR treatment arms.

About IMBRUVICA®

IMBRUVICA® is a once-daily, first-in-class Bruton's tyrosine kinase (BTK) inhibitor that is administered orally, and is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company. IMBRUVICA® blocks the BTK protein; the BTK protein sends important signals that tell B cells to mature and produce antibodies. BTK signaling is needed by specific cancer cells to multiply and spread.[2,3] By blocking BTK, IMBRUVICA® may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow and other organs.[4]

IMBRUVICA® is the most comprehensively studied BTK inhibitor, with more than 150 ongoing clinical trials and five Phase 3 studies supporting the U.S. label. Ongoing clinical trials for IMBRUVICA® include six pivotal Phase 3 trials in CLL, including more than five years of efficacy, safety and tolerability data. It is also the only BTK inhibitor with long-term data in the U.S. label demonstrating progression-free survival in large randomized clinical trials.

IMBRUVICA® is approved in more than 95 countries for at least one indication, and, to date, has been used to treat more than 195,000 patients worldwide across approved indications. It was first approved by the U.S. Food and Drug Administration (FDA) in November 2013 and today is indicated in six disease areas, including five hematologic cancers – chronic lymphocytic leukemia (CLL) with or without 17p deletion (del17p), small lymphocytic lymphoma (SLL) with or without del 17p, Waldenström's macroglobulinemia (WM), previously treated patients with mantle cell lymphoma (MCL)**, previously treated patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior

anti-CD20-based therapy** – and previously treated patients with chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy.[5]

*** Accelerated approval was granted for MCL and MZL based on overall response rate. Continued approval for MCL and MZL may be contingent upon verification and description of clinical benefit in confirmatory trials.*

As of early 2019, the National Comprehensive Cancer Network® (NCCN®), a not-for-profit alliance of 28 leading cancer centers devoted to patient care, research and education, recommends ibrutinib (IMBRUVICA®) as a preferred regimen for the initial treatment of CLL/SLL; and it is the only Category 1 single-agent regimen for treatment-naïve patients without del 17p. The NCCN also updated its guidelines as of February 2020 to elevate IMBRUVICA® with or without rituximab from "other recommended regimens" to a "preferred regimen" for the treatment of relapsed/refractory MCL.

IMBRUVICA® is the only FDA-approved medicine in WM and cGVHD. IMBRUVICA® has been granted four Breakthrough Therapy Designations by the FDA, and it was one of the first medicines to receive U.S. approval with the Breakthrough Therapy Designation.

For more information, visit www.IMBRUVICA.com.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: Fatal bleeding events have occurred in patients who received IMBRUVICA®. Major hemorrhage (≥ Grade 3, serious, or any central nervous system events; e.g., intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post procedural hemorrhage) occurred in 4% of patients, with fatalities occurring in 0.4% of 2,838 patients who received IMBRUVICA® in 27 clinical trials. Bleeding events, including bruising and petechiae, occurred in 39% of patients who received IMBRUVICA®.

The mechanism for the bleeding events is not well understood.

Use of either anticoagulant or antiplatelet agents concomitantly with IMBRUVICA® increases the risk of major hemorrhage. Across clinical trials, 3.1% of 2,838 patients who received IMBRUVICA® without antiplatelet or anticoagulant therapy experienced major hemorrhage. The addition of antiplatelet therapy with or without anticoagulant therapy increased this percentage to 4.4%, and the addition of anticoagulant therapy with or without antiplatelet therapy increased this percentage to 6.1%. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA®. Monitor for signs and symptoms of bleeding.

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 (including bacterial, viral, or fungal) have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 21% of 1,476 patients who received IMBRUVICA® in clinical trials. Cases of progressive multifocal leukoencephalopathy (PML) and Pneumocystis jirovecii pneumonia (PJP) have occurred in patients treated with IMBRUVICA®. Consider prophylaxis according to standard of care in patients who are at increased risk for opportunistic infections.

Monitor and evaluate patients for fever and infections and treat appropriately.

Cytopenias: In 645 patients with B-cell malignancies who received IMBRUVICA® as a single agent, Grade 3 or 4 neutropenia occurred in 23% of patients, Grade 3 or 4 thrombocytopenia in 8% and Grade 3 or 4 anemia in 3%, based on laboratory measurements.

Monitor complete blood counts monthly.

Cardiac Arrhythmias: Fatal and serious cardiac arrhythmias have occurred with IMBRUVICA®. Grade 3 or greater ventricular tachyarrhythmias occurred in 0.2% of patients and Grade 3 or greater atrial fibrillation and atrial flutter occurred in 4% of 1,476 patients who received IMBRUVICA® in clinical trials. These events have occurred particularly in patients with cardiac risk factors, hypertension, acute infections, and a previous history of cardiac arrhythmias.

Periodically monitor patients clinically for cardiac arrhythmias. Obtain an ECG for patients who develop arrhythmic symptoms (e.g., palpitations, lightheadedness, syncope, chest pain) or new onset dyspnea. Manage cardiac arrhythmias appropriately, and if it persists, consider the risks and benefits of IMBRUVICA® treatment and follow dose modification guidelines

Hypertension: Hypertension occurred in 19% of 1,476 patients who received IMBRUVICA® in clinical trials. Grade 3 or greater hypertension occurred in 8% of patients. Based on data from 1,124 of these patients, the median time to onset was 5.9 months (range, 0.03 to 24 months).

Monitor blood pressure in patients treated with IMBRUVICA® and initiate or adjust anti-hypertensive medication throughout treatment with IMBRUVICA® as appropriate.

Second Primary Malignancies: Other malignancies (10%), including non-skin carcinomas (4%), occurred among the 1,476 patients who received IMBRUVICA® in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer (6%).

Tumor Lysis Syndrome: Tumor lysis syndrome has been infrequently reported with IMBRUVICA®. Assess the baseline risk (e.g., 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 pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMBRUVICA® and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during the same time period.

ADVERSE REACTIONS

B-cell malignancies: The most common adverse reactions (≥30%) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were thrombocytopenia (54.5%)*, diarrhea (43.8%), fatigue (39.1%), musculoskeletal pain (38.8%), neutropenia (38.6%)*, rash (35.8%), anemia (35.0%)*, and bruising (32.0%).

The most common Grade ≥ 3 adverse reactions (≥5%) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were neutropenia (20.7%)*, thrombocytopenia (13.6%)*, pneumonia (8.2%), and hypertension (8.0%).

Approximately 9% (CLL/SLL), 14% (MCL), 14% (WM) and 10% (MZL) of patients had a dose reduction due to adverse reactions. Approximately 4-10% (CLL/SLL), 9% (MCL), and 7% (WM [5%] and MZL [13%]) of patients discontinued due to adverse reactions.

cGVHD: The most common adverse reactions (≥20%) in patients with cGVHD were fatigue (57%), bruising (40%), diarrhea (36%), thrombocytopenia (33%)*, muscle spasms (29%), stomatitis (29%), nausea (26%), hemorrhage (26%), anemia (24%)*, and pneumonia (21%).

The most common Grade 3 or higher adverse reactions (≥5%) reported in patients with cGVHD were pneumonia (14%), fatigue (12%), diarrhea (10%), neutropenia (10%)*, sepsis (10%), hypokalemia (7%), headache (5%), musculoskeletal pain (5%), and pyrexia (5%).

Twenty-four percent of patients receiving IMBRUVICA® in the cGVHD trial discontinued treatment due to adverse reactions. Adverse reactions leading to dose reduction occurred in 26% of patients.

*Treatment-emergent decreases (all grades) were based on laboratory measurements.

DRUG INTERACTIONS

CYP3A Inhibitors: Co-administration of IMBRUVICA® with strong or moderate CYP3A inhibitors may increase ibrutinib plasma concentrations. Dose modifications of IMBRUVICA® may be recommended when used concomitantly with posaconazole, voriconazole, and moderate CYP3A inhibitors. Avoid concomitant use of other strong CYP3A inhibitors. Interrupt IMBRUVICA® if strong inhibitors are used short-term (e.g., for ≤ 7 days). See dose modification guidelines in USPI sections 2.4 and 7.1.

CYP3A Inducers: Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment (based on Child-Pugh criteria)**:** Avoid use of IMBRUVICA® in patients with severe baseline hepatic impairment. In patients with mild or moderate impairment, reduce recommended IMBRUVICA® dose and monitor more frequently for adverse reactions of IMBRUVICA®.

Please click here for full Prescribing Information.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of

medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

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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 IMBRUVICA® (ibrutinib). 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., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions 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 29, 2019, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, 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 nor 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] Project Orbis. U.S. Food and Drug Administration. https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis. Accessed April 2020.
[2] Genetics Home Reference. Isolated growth hormone deficiency. http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency. Accessed April 2020.
[3] Turetsky A, et al. Single cell imaging of Bruton's tyrosine kinase using an irreversible inhibitor. *Scientific Reports*. 2014;6:4782.
[4] de Rooij MF, Kuil A, Geest CR, et al. The clinically active BTK inhibitor PCI-32765 targets B-cell receptor- and chemokine-controlled adhesion and migration in chronic lymphocytic leukemia. *Blood*. 2012;119(11):2590-2594.
[5] IMBRUVICA U.S. Prescribing Information, April 2020.