News Release

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Disease-Free Survival Data from CAPTIVATE Study Demonstrate Benefit of IMBRUVICA® (ibrutinib)-Based Regimen as Fixed Duration, First-Line Treatment for Patients with Chronic Lymphocytic Leukemia

New data from the double-blind, placebo-controlled, randomized phase of the Phase 2 CAPTIVATE study presented at ASH 2020 showed that 95 percent of patients with undetectable minimal residual disease randomized to discontinue active treatment after twelve cycles of treatment with IMBRUVICA® plus venetoclax were disease-free and alive, supporting a fixed duration treatment approach

December 5, 2020 (RARITAN, N.J.) – New data from the Phase 2 CAPTIVATE study were presented today during an oral session at the 2020 American Society of Hematology (ASH) Annual Meeting (Abstract #123). The study evaluated the efficacy and safety of IMBRUVICA® (ibrutinib) plus venetoclax in the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) and showed that, after achieving undetectable minimal residual disease (uMRD) in both the blood and bone marrow with the IMBRUVICA® combination regimen, the one-year disease-free survival (DFS) of patients randomized to discontinue active treatment was comparable to that of patients randomized to continue IMBRUVICA® monotherapy (95.3 percent vs. 100 percent, respectively [p=0.1475]).[1] These data, presented by the Janssen Pharmaceutical

Companies of Johnson & Johnson, show the synergistic effect of these two therapies and their combined potential to clear disease from peripheral blood (PB) and bone marrow (BM).[1]

"These data demonstrate the potential of this all-oral, once-daily, chemotherapy-free combination regimen in first-line treatment of CLL," said William Wierda, M.D., Professor, Department of Leukemia, The University of Texas MD Anderson Cancer Center and principal study investigator. "Once-daily treatment with ibrutinib remains the established standard of care in CLL; the latest results from the CAPTIVATE study underscore that the mechanistic synergy of IMBRUVICA® and venetoclax delivers deep MRD remissions in the blood and bone marrow and enables treatment-free periods for patients."

The Phase 2 CAPTIVATE clinical trial (PCYC-1142) is evaluating adult patients younger than 70 years, including patients with high-risk disease, in two cohorts: an MRD Guided Cohort where treatment duration is guided by the patient's MRD status after 12 cycles of combination IMBRUVICA plus venetoclax therapy; and a Fixed Duration Cohort where all patients stop therapy after 12 cycles of the combination, regardless of MRD status. Patients in the MRD Guided Cohort (N=164; median age, 58 years) who achieved uMRD, defined as having uMRD ($<10^{-4}$ by 8-color flow cytometry) serially over at least three cycles and undetectable MRD in both PB and BM with combination therapy, were randomized in a double-blinded fashion to continue treatment with IMBRUVICA® monotherapy or placebo until disease progression.[1]

Patients in the MRD Guided Cohort who did not achieve uMRD following 12 cycles of combination IMBRUVICA plus venetoclax therapy were randomized to continue IMBRUVICA monotherapy or the combination.[1] With a median total treatment duration of 28.6 months, increases in uMRD rates were greater with continued combination therapy versus continued IMBRUVICA monotherapy. Across all 4 randomized arms, 30-month progression-free survival rates were 95 percent or greater.[1]

The safety profile of the IMBRUVICA® plus venetoclax regimen was consistent with known safety profiles of IMBRUVICA® and venetoclax.[1] Across all treated patients, most common grade 3/4 adverse events (AEs) were neutropenia (36 percent), hypertension (10 percent), thrombocytopenia (5 percent), and diarrhea (5 percent).[1]

"IMBRUVICA is the only Bruton's tyrosine kinase inhibitor that has shown significant overall survival and progression-free survival benefits in randomized Phase 3 studies in first-line CLL, and it continues to demonstrate efficacy and safety across regimens and patient subgroups, including those with historically poor outcomes," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "Results from the randomized phase of the MRD Guided Cohort of the CAPTIVATE study confirm that treatment-free remissions are possible with IMBRUVICA-based fixed duration therapy, providing yet another treatment option for patients starting first-line CLL treatment."

The registrational Phase 3 GLOW study, assessing IMBRUVICA plus venetoclax in comparison to chlorambucil plus obinutuzumab for first-line treatment of elderly or younger unfit patients with CLL or SLL (NCT03462719) is ongoing as part of the comprehensive development program exploring the potential of IMBRUVICA-based fixed duration therapy.

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 100 countries for at least one indication, and, to date, has been used to treat more than 200,000 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. 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.

IMBRUVICA® 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.

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 2.3 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.

Learn more at www.janssen.com. Follow us at @JanssenGlobal and @JanssenUS. Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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 and the potential benefits and treatment impact of 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 Research & Development, LLC or 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] Weirda W.G. et al. Ibrutinib (Ibr) Plus Venetoclax (Ven) for First-Line Treatment of Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL): 1-Year Disease-Free Survival (DFS) Results From the MRD Cohort of the Phase 2 CAPTIVATE Study. 2020 *American Society of Hematology Annual Meeting*. December 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.