Media Inquiries:
Christie Corbett
+1 857-636-0211

Bernadette King
+1 215-778-3027

Investor Relations:
Jessica Moore
+1 732-524-2955

U.S. Medical Inquiries:
+1 800-526-7736

New Data from Phase 3 GLOW Study Show Fixed-Duration Treatment with IMBRUVICA® (ibrutinib) Plus Venetoclax Demonstrated Deeper and Sustained Undetectable Minimal Residual Disease Outcomes in First-Line Chronic Lymphocytic Leukemia

Updated results from the MRD cohort of the Phase 2 CAPTIVATE study also highlight potential for treatment-free remissions with IMBRUVICA® plus venetoclax in an oral presentation at ASH 2021

ATLANTA, Ga., December 11, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new data from two studies evaluating the efficacy and safety of IMBRUVICA® (ibrutinib) plus venetoclax (I+V) as a potential fixed-duration treatment in adult patients with previously untreated chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). These data were both featured today during the American Society of Hematology (ASH) 2021 Annual Meeting. New secondary endpoint data from the Phase 3 GLOW study (NCT03462719) showed that fixed-duration treatment with I+V resulted in undetectable minimal residual disease (uMRD) responses that were deeper compared to patients treated with chlorambucil plus obinutuzumab (Clb+O), and an

additional analysis showed that uMRD responses were better sustained during the first year post-treatment.[1]

Updated results from the Phase 2 CAPTIVATE study (NCT02910583) of the same investigational regimen, now with a median 38 months of follow-up, further demonstrated sustained uMRD and disease-free survival (DFS).[2] There were no new MRD relapses, clinical progressions or deaths with an additional year of study follow-up in patients with confirmed uMRD following 12 cycles of combined I+V who were randomized to placebo or continued IMBRUVICA®.[2]

"GLOW and CAPTIVATE are part of a comprehensive development program continuing to evaluate the potential of IMBRUVICA-based therapy in patients with previously untreated CLL with various needs and risk factors, including those with high-risk disease," said Craig Tendler, M.D., Global Head of Late Development, Diagnostics and Medical Affairs, Hematology & Oncology, Janssen Research & Development, LLC. "With data from these two studies showing patients can achieve deep responses with this novel IMBRUVICA plus venetoclax combination, we believe this all-oral, once-daily, fixed-duration regimen offers patients the potential for treatment-free remissions and physicians the flexibility to use IMBRUVICA alone or as a combination therapy to meet the different goals and needs of patients."

Data on MRD Outcomes After Fixed-Duration IMBRUVICA® Plus Venetoclax from the GLOW Study (Abstract #70)

The Phase 3 GLOW study is a randomized, open-label trial which evaluated the efficacy and safety of first-line, fixed-duration I+V vs. Clb+O in elderly patients (≥65 years of age) with CLL/SLL, or patients ages 18-64 with a cumulative illness rating scale (CIRS) score of greater than six or creatinine clearance less than 70 mL/min, without del(17p) or known *TP53* mutations.[1] Patients in the study were randomized to receive either I+V (n= 106) or Clb+O (n=105).[1] Previously reported data were presented at the 2021 European Hematology Association (EHA) Virtual Congress and showed that the study met its primary endpoint of progression-free survival (PFS) as measured by an independent review committee (IRC).[3]

The prespecified secondary endpoint was rate of uMRD (uMRD < 10^{-4}). MRD was evaluated via next-generation sequencing (NGS) and reported with cutoffs of < 10^{-4} and < 10^{-5}. Rate of uMRD was reported at three and 12 months after end of treatment in both study arms.[1]

The data presented at ASH demonstrated deeper responses at end of treatment and better sustained uMRD responses during the first year post-treatment with all-oral, once-daily fixed-duration I+V vs. Clb+O.[1] Further, responses were proportionally deeper at the level of < 10^{-5} in the I+V arm vs. Clb+O arm in both peripheral blood (PB) and bone marrow (BM).[1]

"The GLOW study combines two highly active blood cancer treatments that act in a synergistic fashion by complementary mechanisms to deliver superior progression-free survival in the first-line treatment of CLL," said Arnon Kater†, M.D., Ph.D., Deputy Head of Hematology, Amsterdam University Medical Centers, University of Amsterdam and Chairman of the HOVON CLL Working Group, the Netherlands and principal study investigator. "These latest results show the potential to provide treatment-free remissions for patients through robust disease clearance in lymphoid tissue, blood and bone marrow, and early sustainability of those responses after stopping treatment."

GLOW Results:

- With updated median follow-up of 34.1 months, the 30-month PFS was 80.5 percent with I+V vs. 35.8 percent for Clb+O.[1]
- Rates of uMRD < 10^{-5} were higher with I+V vs. Clb+O in BM (40.6 percent vs. 7.6 percent) and in PB (43.4 percent vs. 18.1 percent).[1]
    - With I+V, deep responses < 10^{-5} were seen in patients with unmutated IGHV CLL, and depth of response was mirrored in PB (49.1 percent) and BM (45.5 percent).[1]
- An additional analysis evaluated sustainability of uMRD response between three and 12 months following end of treatment; 80.4 percent of patients with I+V had sustained uMRD < 10^{-5} vs. 26.3 percent with Clb+O.[1]

- PFS rate during the first-year post-treatment was sustained >90 percent with I+V, independent of BM or PB MRD status three months after end of treatment.[1]
- Additional follow-up is warranted to confirm the long-term impact of MRD status on PFS.[1]

Data from the MRD Cohort of the Phase 2 CAPTIVATE (PCYC-1142) Study (Abstract #68)

The Phase 2 CAPTIVATE trial evaluated 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 I+V therapy; and a fixed-duration cohort where all patients stop therapy after 12 cycles of the combination, regardless of MRD status.[2] The primary endpoints of the study included MRD negative response rate, DFS, and complete response rate. Data from the primary analysis from both the fixed-duration and MRD-guided cohorts were previously reported.[4,5] Patients with high-risk disease included unmutated IGHV (60 percent of patients), del(17p)/*TP53* mutation (20 percent), complex karyotype (19 percent), and del(11q) without del(17p) (17 percent).[2] 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 uMRD 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.[2] Patients in the MRD-guided cohort who did not achieve uMRD following 12 cycles of combination I+V therapy were randomized to continue IMBRUVICA® monotherapy or the combination.[2]

DFS was defined as freedom from MRD relapse ($\geq 10^{-2}$ confirmed on two separate occasions) and without progressive disease or death starting from randomization after 15 cycles of treatment.[2] The two-year DFS rates post-randomization with time-limited treatment (randomized to placebo) was maintained at 95 percent with an additional year of study follow-up. There were no new MRD relapses, disease

progressions, or deaths in patients with confirmed uMRD treated with placebo or IMBRUVICA®.[2] Early data suggest that patients who progress after time-limited treatment with I+V have the potential to be successfully retreated with single-agent IMBRUVICA®.[2]

Additionally, the estimated 36-month PFS rates were 95.3 percent with placebo and 100 percent with IMBRUVICA® (95 percent Confidence Interval [CI], 4.7 percent difference, -1.6–10.9, overall log-rank *P*=0.1573); placebo 82.7–98.8, IMBRUVICA® 100–100).[2] Ultimately, these results in patients randomized to placebo following an initial 12 cycles of the I+V combination support the potential for treatment-free remission with first-line, fixed-duration I+V, an all-oral, once-daily regimen.[2] Among 12 patients who progressed after fixed-duration treatment, nine patients with available responses all had a partial response to single-agent IMBRUVICA® with limited follow-up; three have pending responses.[2]

With a median study follow-up of 38 months, the safety profile of the I+V regimen in CAPTIVATE was consistent with known safety profiles of IMBRUVICA® and venetoclax.[2] The most common AEs of any Grade 13-24 months post-randomization were arthralgia (29 percent I+V; 22 percent IMBRUVICA® monotherapy) and upper respiratory tract infection (20 percent I+V; 15 percent IMBRUVICA® monotherapy).[2] Grade ≥3 adverse events (AEs) were infrequent across randomized arms with the exception of neutropenia.[2]

About IMBRUVICA®

IMBRUVICA® (ibrutinib) is a once-daily oral medication that is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company. IMBRUVICA® blocks the Bruton's tyrosine kinase (BTK) protein, which is needed by normal and abnormal B cells, including specific cancer cells, to multiply and spread. By blocking BTK, IMBRUVICA® may help move abnormal B cells out of their nourishing environments and inhibits their proliferation.[6,7,8]

IMBRUVICA® is approved in more than 100 countries and has been used to treat more than 250,000 patients worldwide. There are more than 50 company-

sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of IMBRUVICA®.

IMBRUVICA® was first approved by the U.S. Food and Drug Administration (FDA) in November 2013, and today is indicated for adult patients in six disease areas, including five hematologic cancers. These include indications to treat adults with CLL/SLL with or without 17p deletion (del17p), and adults with Waldenström's macroglobulinemia (WM), and adult patients with previously treated mantle cell lymphoma (MCL)*, as well as to treat adult patients with previously treated marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy*, and adult patients with previously treated chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy.[9]

**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.*

Since 2019, the National Comprehensive Cancer Network® (NCCN®), recommends ibrutinib (IMBRUVICA®) as a preferred regimen for the initial treatment of CLL/SLL and has Category 1 treatment status for treatment-naïve patients without deletion 17p/*TP53* mutation and as a preferred treatment for treatment-naïve patients with deletion 17p/*TP53* mutation. The NCCN Guidelines also recommend IMBRUVICA®, with or without rituximab, as a preferred regimen for the treatment of relapsed/refractory MCL, as a Category 1 preferred regimen for both untreated and previously treated WM patients, and as a preferred regimen for relapsed/refractory MZL.[10]

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 postprocedural 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 of any grade including bruising and petechiae occurred in 39%, and excluding bruising and petechiae occurred in 23% of patients who received IMBRUVICA®, respectively.

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 and Cardiac Failure: Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Grade 3 or greater ventricular tachyarrhythmias occurred in 0.2% of patients, Grade 3 or greater atrial fibrillation and atrial flutter occurred in 4%, and Grade 3 or greater cardiac failure occurred in 1% 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.

At baseline and then periodically, monitor patients clinically for cardiac arrhythmias and cardiac failure. Obtain an ECG for patients who develop arrhythmic symptoms (e.g., palpitations, lightheadedness, syncope, chest pain) or new onset dyspnea. Manage cardiac arrhythmias and cardiac failure 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 2.3 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 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** to see the 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 @JanssenUS and @JanssenGlobal. Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

†Dr. Kater has served as a consultant to Janssen; he has not been paid for any media work.

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, Janssen Biotech, Inc., 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 January 3, 2021, 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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