News Release

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New Results from the Phase 3 GLOW Study of Fixed-Duration Treatment with IMBRUVICA® (ibrutinib) Plus Venetoclax Demonstrate Robust Efficacy and Sustained Response in Older, Unfit Patients with Previously Untreated Chronic Lymphocytic Leukemia

With nearly four years of study follow-up, all-oral, fixed duration IMBRUVICA® + venetoclax reduced the risk of progression or death by 79 percent and demonstrated overall survival (OS) advantage versus chemoimmunotherapy

NEW ORLEANS, December 10, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new four-year follow-up results from the Phase 3 GLOW study (Abstract #93), which showed investigational, fixed-duration treatment with IMBRUVICA® + venetoclax (I+V) reduced the risk of progression or death by 79 percent among older and/or unfit patients with previously untreated chronic lymphocytic leukemia (CLL) compared to patients treated with chemoimmunotherapy.[1] These results were highlighted in an oral presentation during the 2022 American Society of Hematology (ASH) Annual Meeting.[1]

CLL is the most common form of leukemia in adults in the U.S. and currently has no cure.[2] While the treatment landscape has evolved significantly since the emergence of targeted agents, there is still significant unmet need for novel treatment options, including fixed-duration regimens.

"The GLOW study results demonstrate the potential of fixed-duration I+V to become an additional treatment option for older, unfit patients with CLL in the first-line setting, and this fixed-dose combination may offer a flexible regimen for patients seeking a time-limited treatment approach," said study investigator Carsten Niemann,† M.D., Ph.D., Clinical Associate Professor and Principal Investigator at Rigshospitalet, Copenhagen, Denmark. "This first all-oral, fixed-duration novel combination demonstrates an OS advantage in the first-line treatment of CLL and is an innovative option for patients."

In the study, fixed-duration I+V therapy exhibited robust efficacy in older and/or unfit adults with previously untreated CLL, with a superior and sustained benefit in progression-free survival (PFS) with four years of follow-up.[1] Seventy-five percent of patients treated with the combination were alive and progression-free at 3.5 years.[1] I+V also demonstrated an OS advantage versus chlorambucil plus obinutuzumab (Clb+O) at this latest study follow-up.[1] Exploratory analyses showed that post-treatment PFS rates were higher for I+V (n=106) than Clb+O (n=105), regardless of minimal residual disease (MRD) status post-treatment.[1]

GLOW Results

- With a median 46 months of follow-up, I+V reduced the risk of disease progression or death by 79 percent versus Clb+O (Hazard Ratio (HR) 0.214; [95 percent Confidence Interval (CI), 0.138-0.334]; $p<0.0001$).[1]
- I+V is the first fixed-duration novel combination to demonstrate an OS advantage compared to Clb+O in the first-line treatment of CLL (HR 0.487; [95 percent CI, 0.262-0.907]; nominal $p=0.0205$).[1]
- An estimated 74.6 percent of previously untreated older and/or comorbid patients were alive and progression-free at 3.5 years with all-oral, once-daily, fixed-duration I+V treatment compared to an estimated 24.8 percent of patients in the Clb+O cohort.[1]
    - PFS at 3.5 years was higher for patients in the I+V arm compared to the Clb+O arm for both unmutated IGHV (uIGHV) and mutated IGHV (mIGHV) CLL. [1]
    - PFS was better sustained in the I+V arm compared to the Clb+O arm, regardless of MRD ($\geq 10^{-4}$) status, measured at three months following end of treatment.[1]
    - Two years after end of treatment, estimated PFS was ≥ 90 percent for patients with mIGHV CLL, independent of MRD status, and for the 60 percent of patients with uIGHV CLL who achieved undetectable MRD (uMRD).[1]

Updated data for both studies showed the safety profile of the I+V regimen was consistent with known safety profiles of IMBRUVICA® and venetoclax.[1]

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"IMBRUVICA has helped change the standard of care for adults living with CLL and other B-cell malignancies, and this study adds to the extensive body of evidence supporting its potential to provide improved survival for patients with CLL. These results highlight the potential for front-line CLL patients to be treated with an all-oral, fixed-duration treatment," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Janssen Research & Development, LLC. "At Janssen, we are committed to addressing the unmet needs of patients with CLL through continued investment in our IMBRUVICA clinical development program."

In addition to the GLOW results, data from the Phase 2 CAPTIVATE study of the MRD cohort (PCYC-1142) (Abstract #92), which utilized the same I+V schedule for the first 15 cycles as in the GLOW study, were also presented in an oral session at ASH.[3] After the first 15 cycles, patients with confirmed uMRD (n=86) were randomized to IMBRUVICA® or placebo.[3] Disease-free survival at three years post-randomization was 93 percent for IMBRUVICA® and 85 percent for placebo.[3] PFS rates at four years from start of treatment were 95 percent and 88 percent, respectively, and OS rates were 98 percent and 100 percent.[3]

During the three-year post-randomization period, no new atrial fibrillation events occurred in the placebo arm, and no new grade three or higher hemorrhage events occurred in either arm.[3] The incidences of hypertension, arthralgia, neutropenia and diarrhea were generally infrequent in the placebo arm during this time period.[3] No deaths occurred in either arm during the last 12 months of follow-up.[3]

About GLOW

The GLOW study (NCT03462719) is a randomized, open-label, Phase 3 trial that evaluated the efficacy and safety of first-line, fixed-duration I+V versus 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, who had active disease requiring treatment per the International Workshop on CLL (iwCLL) criteria.[4] Patients with del(17p) or known TP53 mutations were excluded.[4] There were 211 patients randomly assigned in a 1:1 ratio to receive either I+V (n=106) and or Clb+O (n=105) and the median age was 71 years.[4] Patients assigned to I+V received treatment for 15 cycles (1 cycle is 28 days), starting with three cycles of IMBRUVICA® monotherapy lead-in followed

by the combination of I+V for 12 cycles.[4] Patients assigned to Clb+O were treated for six cycles.[4]

Among patients with partial response or better, MRD in peripheral blood (PB) was evaluated using next-generation sequencing (NGS) via clonoSEQ on-treatment and at 3-6 month intervals post-treatment.[4] ClonoSEQ data was used as part of CLL clonal testing.[4]

The primary endpoint was PFS up to two years and 10 months.[4] Secondary endpoints of the study include MRD negative rate, compete response rate, overall response rate, OS, duration of response and time-to-next treatment.[4]

About CAPTIVATE

The Phase 2 CAPTIVATE study (NCT02910583) evaluated previously untreated adult patients with CLL who were 70 years or younger, including patients with high-risk disease, in two cohorts: an MRD-guided cohort (n=164; median age, 58 years) and a fixed-duration cohort (n=159; median age, 60 years).[5] Patients received three cycles of IMBRUVICA® lead-in followed by 12 cycles of I+V (oral IMBRUVICA® [420 mg/d]; oral venetoclax [five-week ramp-up to 400 mg/d]) and the primary endpoint was one-year disease-free survival.[5] In this MRD cohort, after completion of I+V, patients with confirmed uMRD were randomly assigned to double-blind treatment with placebo (i.e., a fixed-duration regimen), or continuous IMBRUVICA®.[5]

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 270,000 patients worldwide. There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, more than 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 chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL) with or without 17p deletion (del17p); adults with Waldenström's macroglobulinemia (WM); adult patients with previously treated mantle cell lymphoma (MCL)*; 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 and pediatric patients aged one year and older 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.*

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 4.2% 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.

Cardiac Arrhythmias, Cardiac Failure, and Sudden Death: Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Deaths due to cardiac causes or sudden deaths occurred in 1% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These adverse reactions occurred in patients with and without preexisting hypertension or cardiac comorbidities. Patients with cardiac comorbidities may be at greater risk of these events.

Grade 3 or greater ventricular tachyarrhythmias were reported in 0.2%, Grade 3 or greater atrial fibrillation and atrial flutter were reported in 3.7%, and Grade 3 or greater cardiac failure was reported in 1.3% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These events have occurred particularly in patients with cardiac risk factors including hypertension and diabetes mellitus, a previous history of cardiac arrhythmias, and in patients with acute infections.

Evaluate cardiac history and function at baseline, and monitor patients for cardiac arrhythmias and cardiac function. Obtain further evaluation (e.g., ECG, echocardiogram) as indicated for patients who develop symptoms of arrhythmia (e.g., palpitations, lightheadedness, syncope, chest pain), new onset dyspnea, or other cardiovascular concerns. Manage cardiac arrhythmias and cardiac failure appropriately, follow dose modification guidelines, and consider the risks and benefits of continued IMBRUVICA®

treatment.

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®, initiate or adjust anti-hypertensive medication throughout treatment with IMBRUVICA® as appropriate, and follow dosage modification guidelines for Grade 3 or higher hypertension.

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 2.8%, based on laboratory measurements. Monitor complete blood counts monthly.

Second Primary Malignancies: Other malignancies (10%), including non-skin carcinomas (3.9%), 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 adult 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 adult 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 adult 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 adult or pediatric patients with cGVHD were fatigue (57%), anemia (49%)*, bruising (40%), diarrhea (36%), thrombocytopenia (33%)*, musculoskeletal pain (30%), pyrexia (30%), muscle spasms (29%), stomatitis (29%), hemorrhage (26%), nausea (26%), abdominal pain (23%), pneumonia (23%), and headache (21%).

The most common Grade 3 or higher adverse reactions (≥5%) reported in adult or pediatric patients with cGVHD were pneumonia (14%), anemia (13%)*, fatigue (12%), pyrexia (11%), diarrhea (10%), neutropenia (10%)*, sepsis (10%), osteonecrosis (9%), stomatitis (9%), hypokalemia (7%), headache (5%), and musculoskeletal pain (5%).

Discontinuation of IMBRUVICA® treatment due to an adverse reaction occurred in 24% of adult patients and 23% of pediatric patients. Adverse reactions leading to dose reduction occurred in 26% of adult patients and 19% of pediatric 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. Increased ibrutinib concentrations may increase the risk of drug-related toxicity. Dose modifications of IMBRUVICA® are 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). Avoid grapefruit and Seville oranges during IMBRUVICA® treatment, as these contain strong or moderate inhibitors of CYP3A. See dose modification guidelines in USPI sections 2.3 and 7.1.

CYP3A Inducers: Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Pediatric Use: The safety and effectiveness of IMBRUVICA® have not been established for the treatment of cGVHD after failure of one or more lines of therapy in pediatric patients less than 1 year of age. The safety and effectiveness of IMBRUVICA® in pediatric patients have not been established in MCL, CLL/SLL, CLL/SLL with 17p deletion, WM, MZL or in patients with mature B-cell non-Hodgkin lymphoma.

In the randomized population from a study that included 35 patients (26 pediatric patients age 5 to less than 17 years) with previously treated mature B-cell non-Hodgkin lymphoma, major hemorrhage and discontinuation of chemoimmunotherapy due to adverse reactions occurred more frequently in the ibrutinib plus chemoimmunotherapy arm compared to the chemoimmunotherapy alone arm.

Hepatic Impairment:

Adult Patients with B-cell Malignancies: 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®.

Patients with cGVHD: Avoid use of IMBRUVICA® in patients with total bilirubin level > 3x upper limit of normal (ULN) (unless of non-hepatic origin or due to Gilbert's syndrome). Reduce recommended dose when administering IMBRUVICA® to patients with total bilirubin level > 1.5 to 3x ULN (unless of non-hepatic origin or due to Gilbert's syndrome).

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 & Retina; 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.

†Dr. Niemann 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 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Reports on Form 10-Q, and other 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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