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New Phase 3 Study Findings Show IMBRUVICA® (ibrutinib) Plus Rituximab Significantly Improved Survival Compared to Fludarabine, Cyclophosphamide, and Rituximab (FCR) in Previously Untreated Patients Aged 70 or Younger with Chronic Lymphocytic Leukemia

- *First head-to-head trial showing greater safety and efficacy of IMBRUVICA-based therapy versus FCR*
- *Results from this interim analysis featured as a Late-Breaker at ASH 2018 (abstract #LBA-4)*

SAN DIEGO, December 4, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today results from the National Cancer Institute (NCI)-sponsored Phase 3 study (E1912) led by the ECOG-ACRIN Research Group (ECOG-ACRIN) evaluating IMBRUVICA® (ibrutinib) plus rituximab compared to a chemotherapy regimen of fludarabine, cyclophosphamide, and rituximab (FCR) in previously untreated patients aged 70 years or younger with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).[1]

With nearly three years of follow-up, the data showed IMBRUVICA plus rituximab significantly prolonged progression-free survival (PFS) and overall survival (OS) versus FCR.

The findings were presented during the Late-Breaker abstract oral session at the 60th American Society of Hematology (ASH) Annual Meeting (abstract #LBA-4). IMBRUVICA, a Bruton's tyrosine kinase (BTK) inhibitor studied in patients with CLL for up to seven years, is jointly developed and commercialized by Janssen Biotech, Inc., and Pharmacyclics LLC, an AbbVie company.[2] The federally funded study was designed by researchers with ECOG-ACRIN. It was conducted through the NCI's National Clinical Trials Network. Pharmacyclics LLC provided ibrutinib under a cooperative research and development agreement with NCI and a separate agreement with ECOG-ACRIN.

"While FCR has long been the most commonly used treatment regimen for younger patients with chronic lymphocytic leukemia, we have been eagerly awaiting a treatment with an improved safety and efficacy profile for these patients," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Janssen Research & Development, LLC. "The results from this Phase 3 head-to-head trial demonstrate the significant treatment benefit of the IMBRUVICA combination versus FCR."

At a median follow-up of 33.4 months, IMBRUVICA plus rituximab showed significantly prolonged PFS compared to FCR in previously untreated patients aged 70 years or younger with CLL/SLL (HR: 0.35; 95 percent confidence interval [CI]: 0.22-0.56; p<0.0001). The study also demonstrated an improved OS for the IMBRUVICA plus rituximab treatment arm versus FCR (HR: 0.17; 95 percent CI: 0.05-0.54; p=0.0003). In a subgroup analysis for PFS, IMBRUVICA plus rituximab showed prolonged PFS independent of age, sex, performance status (0-2), disease stage, or the presence/absence of deletion 11q23.

About the Data Presentation

Abstract #LBA-4: A Randomized Phase III Study of Ibrutinib (PCI-32765)-Based Therapy Vs. Standard Fludarabine, Cyclophosphamide, and Rituximab (FCR) Chemoimmunotherapy in Untreated Younger Patients with Chronic Lymphocytic Leukemia (CLL): A Trial of the ECOG-ACRIN Cancer Research Group (E1912)
Late-Breaker Oral Presentation: Tuesday, December 4 at 7:30am PT

The Phase 3 study (E1912) evaluated previously untreated patients with CLL or SLL aged 70 years or younger who were randomly assigned to receive IMBRUVICA (420 mg/day until disease progression) and rituximab (50 mg/m^2 on day 1 of cycle 2; 325 mg/m^2 on day 2 of cycle 2; 500 mg/m^2 on day 1 of cycles 3-7) (n=354) or six courses of intravenous fludarabine (25 mg/m^2) and cyclophosphamide (250 mg/m^2) days 1-3 with rituximab (50 mg/m^2 on day 1 of cycle 1; 325 mg/m^2 on day 2 of cycle 1; 500 mg/m^2 on day 1 of cycles 2-6) every 28-days (n=175). The primary endpoint was PFS with a secondary endpoint of OS.

With a median follow-up of 33.4 months, the interim analysis observed 77 PFS events and 14 deaths. IMBRUVICA plus rituximab significantly improved PFS compared to FCR (HR: 0.35; 95 percent CI: 0.22-0.56; p<0.0001); the pre-specified boundary for PFS was crossed. The IMBRUVICA plus rituximab treatment arm also showed improved OS (HR: 0.17; 95 percent CI: 0.05-0.54; p=0.0003, pre-specified boundary for superiority p=0.0005).

In a subgroup analysis for PFS, IMBRUVICA plus rituximab showed prolonged PFS independent of age, sex, performance status (0-2), disease stage, or the presence/absence of cytogenetic abnormality, deletion 11q23. With current follow-up, IMBRUVICA plus rituximab was also superior to FCR for IGHV unmutated patients (HR: 0.26; 95 percent CI: 0.14-0.50; p<0.0001) but not IGHV mutated patients (HR: 0.44; 95 percent CI: 0.14-0.135; p=0.07).

Grade 3/4 treatment-related adverse events were observed in 58 percent of IMBRUVICA plus rituximab treated patients and 72 percent of FCR treated patients (p=0.0042). FCR was more frequently associated with Grade 3 and 4 neutropenia (FCR: 44 percent vs. IMBRUVICA plus rituximab: 23 percent; p<0·0001) and infectious complications (FCR: 18 percent vs. IMBRUVICA plus rituximab: 7 percent; p<0.0001).

About IMBRUVICA

IMBRUVICA (ibrutinib) is a first-in-class, once-daily oral medicine that works differently than chemotherapy as it blocks the Bruton's tyrosine kinase (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.[3,4] By blocking BTK, IMBRUVICA may

help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.[5,6]

IMBRUVICA is approved in more than 90 countries, and, to date, has been used to treat more than 135,000 patients worldwide across approved indications. It was first approved by the U.S. Food and Drug Administration in 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 del17p, 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.[6]

IMBRUVICA is the first and only FDA-approved medicine in WM, MZL* 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 through the Breakthrough Therapy Designation.

IMBRUVICA is a comprehensively studied molecule in the oncology industry. The robust clinical oncology development program includes more than 150 active clinical trials studying IMBRUVICA alone and in combination with other medicines in several blood cancers and other serious diseases. For more information, visit www.IMBRUVICA.com.

** 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.*

Additional Information about IMBRUVICA®

INDICATIONS

IMBRUVICA is indicated to treat adults with[3]

- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL)
- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion
- Waldenström's macroglobulinemia (WM)

- Mantle cell lymphoma (MCL) patients who have received at least one prior therapy
    - Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Marginal zone lymphoma (MZL) patients who require systemic therapy and have received at least one prior anti-CD20-based therapy
    - Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Chronic Graft-Versus-Host Disease (cGVHD) patients who failed one or more lines of systemic therapy

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 3% of patients, with fatalities occurring in 0.3% of 1,011 patients exposed to IMBRUVICA® in clinical trials. Bleeding events of any grade, including bruising and petechiae, occurred in 44% 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 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 24% of 1,011 patients exposed to 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: Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (23%), thrombocytopenia (8%), and anemia (3%) based on laboratory measurements occurred in patients with B-cell malignancies treated with single agent IMBRUVICA®.
Monitor complete blood counts monthly.

Cardiac Arrhythmias: Fatal and serious cardiac arrhythmias have occurred with IMBRUVICA® therapy. 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 1,011 patients exposed to 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 has occurred in 12% of 1,011 patients treated with IMBRUVICA® in clinical trials with a median time to onset of 5 months (range, 0.03 to 22 months). Monitor patients for new onset hypertension or hypertension that is not adequately controlled after starting IMBRUVICA®. Adjust existing anti-hypertensive medications and/or initiate anti-hypertensive treatment as appropriate.

Second Primary Malignancies: Other malignancies (9%) including non-skin carcinomas (2%) have occurred in 1,011 patients treated with 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® therapy. 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 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. Advise men to avoid fathering a child during the same time period.

ADVERSE REACTIONS

B-cell malignancies: The most common adverse reactions (≥20%) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were thrombocytopenia (58%)*, neutropenia (58%)*, diarrhea (42%), anemia (39%)*, rash (31%), musculoskeletal pain (31%), bruising (31%), nausea (28%), fatigue (27%), hemorrhage (23%), and pyrexia (20%).

The most common Grade 3 or 4 adverse reactions (≥5%) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were neutropenia (36%)*, thrombocytopenia (15%)*, and pneumonia (10%).

Approximately 6% (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%)*, stomatitis (29%), muscle spasms (29%), nausea (26%), hemorrhage (26%), anemia (24%)*, and pneumonia (21%).
The most common Grade 3 or 4 adverse reactions (≥5%) reported in patients with cGVHD were fatigue (12%), diarrhea (10%), neutropenia (10%)*, pneumonia (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 and adverse reactions.

DRUG INTERACTIONS

CYP3A Inhibitors: Dose adjustments may be recommended.
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 IMBRUVICA® dose.

Please click here for full Prescribing Information.

About the Janssen Pharmaceutical Companies of Johnson & Johnson
At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at @JanssenGlobal and @JanssenUS. Janssen Biotech, Inc. and Janssen Research & Development, LLC 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 a new improved indication for 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, any of the other Janssen Pharmaceutical Companies of Johnson & Johnson 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 31, 2017, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's subsequent most recently filed Quarterly Reports on Form 10-Q and the company's subsequent 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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[1] Shanafelt, et al. ASH 2018 Abstract #LBA-4.
[2] Byrd, et al. ASH 2018 Abstract #3133.
[3] Genetics Home Reference. Isolated growth hormone deficiency. http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency. Accessed December 2018.
[4] Turetsky, et al. Single cell imaging of Bruton's Tyrosine Kinase using an irreversible inhibitor. Scientific Reports. volume 4, Article number: 4782 (2014).
[5] 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.
[6] IMBRUVICA U.S. Prescribing Information, August 2018.