NEWS RELEASE

Ibrutinib (IMBRUVICA®) HELIOS Interim Analysis Study Data Show Significant Reductions in Risk of Progression or Death in Patients with Previously-Treated Chronic Lymphocytic Leukemia

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CHICAGO and RARITAN, NJ, May 30, 2015 - Data from the Phase 3 CLL3001 (HELIOS) trial demonstrated that the combination of ibrutinib (IMBRUVICA®) plus bendamustine and rituximab (BR) reduced the risk of progression or death by 80% and also significantly improved overall response rate (ORR) versus placebo plus BR in patients with relapsed or refractory (R/R) chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL). Janssen Research & Development, LLC (Janssen) today announced these data, which will be included today in the official press program at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL. The data will also be presented in full by the lead author of the study, Dr. Asher Chanan-Khan, based at the Mayo Clinic in Jacksonville, Florida, in an oral, late-breaking abstract session today during the Leukemia, Myelodysplasia, and Transplantation track at 2:27 p.m. CT. IMBRUVICA is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC.

At a pre-planned interim analysis **earlier this year**, the addition of ibrutinib to BR was shown to significantly improve progression-free survival (PFS; the primary endpoint) and ORR (a key secondary endpoint) compared with the combination of BR and placebo. An independent review committee (IRC) recommended HELIOS be unblinded at that point and patients receiving placebo plus BR be offered the option to receive ibrutinib as their next treatment.

"The HELIOS data are particularly exciting, as they demonstrate that ibrutinib combination therapy improved PFS rates three-fold in previously treated patients with CLL or SLL, versus chemo-immunotherapy alone," said Simon

Rule, M.D., Consultant Haematologist, Department of Haematology, and Head of the Lymphoma Service, Derriford Hospital, Plymouth, UK, and HELIOS study investigator. "As clinicians, we have continued to search for safe and effective options for people who have relapsed or become refractory to treatment. These results suggest the combination of ibrutinib, bendamustine and rituximab may be a favorable option for many patients who have received previous therapy."

HELIOS is a Janssen-sponsored, randomized, double-blind, placebo-controlled, international, multicenter Phase 3 study conducted in 21 countries, which evaluated the safety and efficacy of ibrutinib in combination with BR in 578 patients with relapsed or refractory CLL/SLL who had received at least one prior therapy. Patients were randomized to receive either the combination of 420 mg ibrutinib orally once daily and six cycles of BR, or a matching regimen of placebo orally once daily and six cycles of BR, with ibrutinib or placebo continued until disease progression or unacceptable toxicity. The primary endpoint was IRC-assessed PFS and key secondary endpoints included ORR per IRC, overall survival (OS), rate of minimal residual disease negative remissions (MRD- remissions) and safety.

At a median follow-up of 17 months, IRC-assessed PFS was significantly longer with ibrutinib+BR, compared to placebo+BR (median not reached vs. 13.3 months; HR: 0.203, 95% CI: 0.150-0.276, P<0.0001). This difference in PFS rates between study arms was consistent across all subgroups, including high-risk subgroups. IRC-assessed PFS rates at 18 months were 79% for patients in the ibrutinib+BR arm, as compared with 24% for patients in the placebo+BR arm. The IRC-assessed ORR and complete response/complete response with incomplete marrow recovery (CR/CRi) rates were 82.7% and 10.4%, respectively, for patients taking ibrutinib+BR versus 67.8% and 2.8% for people in the placebo+BR arm. The median OS has not yet been reached at a median follow-up of 17 months. Overall, ibrutinib reduced the risk of death by 37% (P=0.06). The OS results are, however, confounded as 90 patients (31%) in the placebo+BR arm with confirmed progressive disease had crossed over to receive ibrutinib and no longer received placebo for the remainder of the trial. The safety profile of ibrutinib+BR was consistent with the known individual safety profiles for ibrutinib and BR therapies, respectively. In addition, ibrutinib had no impact on the ability of BR to be administered, with a similar number of BR cycles administered in both study arms.

"HELIOS represents the first read-out of a Phase 3 study evaluating ibrutinib in combination with standard chemo-immunotherapy. The data demonstrate the potential benefits of ibrutinib when combined with standard therapy for people with previously treated CLL or SLL," said Sen Zhuang, M.D., Ph.D., Vice President, Oncology Clinical Research, Janssen. "Notably, this is the second Phase 3 trial to demonstrate ibrutinib significantly delays progression for previously treated patients with these diseases."

The most common all-grade adverse events (AEs ≥20%) in the HELIOS trial were neutropenia (58.2% in the ibrutinib+BR arm vs. 54.7% in the placebo+BR arm), nausea (36.9% vs. 35.2%), diarrhea (35.5% vs. 23.7%), thrombocytopenia (30.7% vs. 24.4%), pyrexia (24.7% vs. 22%), anemia (22.6% vs. 28.9%) and fatigue (21.6% vs.

22.6%). The most common Grade 3/4 AEs (≥15%) were neutropenia (53.7% vs. 50.5%) and thrombocytopenia (15% in both arms). Higher rates of Grade 1/2 bleeding such as hematoma (8% vs. 1%), contusion (7.7% vs. 3.1%), epistaxis (5.9% vs. 3.1%), ecchymosis (3.1% vs. 0.7%) and petechiae (2.8% vs. 0.3%) were observed in patients taking ibrutinib+BR versus those in the placebo+ BR arm. Rates of major hemorrhage (defined as serious or Grade 3 or greater events) were 3.8% (11 cases) and 1.7% (5 cases), respectively. Few patients had Grade 3/4 atrial fibrillation (8 cases or 2.8% and 2 cases or 0.7%), with most patients having a history of prior atrial fibrillation or cardiac risk factors. Overall, 14.2% of patients in the ibrutinib arm discontinued due to AEs, as compared to 11.8% of patients in the placebo arm. The rates of other malignancies reported during treatment and follow-up were similar in each arm (8.4% in patients taking ibrutinib+BR vs. 8% in patients taking placebo+BR)

A full study report for HELIOS is being prepared and planned to be submitted to health authorities for future labeling considerations. A manuscript is also planned for submission for potential publication in a peer-reviewed journal. For additional study information, visit **ClinicalTrials.gov**.

About IMBRUVICA® (ibrutinib)

IMBRUVICA was one of the first therapies to receive U.S. approval after having received the FDA's Breakthrough Therapy Designation. IMBRUVICA works by blocking a specific protein called Bruton's tyrosine kinase (BTK).[1] The BTK protein transmits important signals that tell B cells to mature and produce antibodies and is needed by specific cancer cells to multiply and spread.[1,2] IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.[1] For more information, visit **www.IMBRUVICA.com**.

Additional Information about IMBRUVICA® INDICATIONS

IMBRUVICA® is indicated to treat people with:

- Mantle cell lymphoma (MCL) 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 of clinical benefit in confirmatory trials.
- Chronic lymphocytic leukemia (CLL) who have received at least one prior therapy
- Chronic lymphocytic leukemia (CLL) with 17p deletion
- Waldenström's macroglobulinemia (WM)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (subdural hematoma, gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half 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. 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 have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 14% to 26% of patients. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA®. Monitor patients for fever and infections and evaluate promptly.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 19 to 29%), thrombocytopenia (range, 5 to 17%), and anemia (range, 0 to 9%) occurred in patients treated with IMBRUVICA®. Monitor complete blood counts monthly.

Atrial Fibrillation - Atrial fibrillation and atrial flutter (range, 6 to 9%) have occurred in patients treated with IMBRUVICA®, particularly in patients with cardiac risk factors, acute infections, and a previous history of atrial fibrillation. Periodically monitor patients clinically for atrial fibrillation. Patients who develop arrhythmic symptoms (e.g., palpitations, lightheadedness) or new-onset dyspnea should have an ECG performed. If atrial fibrillation persists, consider the risks and benefits of IMBRUVICA® treatment and dose modification.

Second Primary Malignancies - Other malignancies (range, 5 to 14%) including non-skin carcinomas (range, 1 to 3%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4 to 11%).

Tumor Lysis Syndrome - Tumor lysis syndrome has been reported with IMBRUVICA® therapy. Monitor patients closely and take appropriate precautions in patients at risk for tumor lysis syndrome (e.g., high tumor burden).

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®. 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.

ADVERSE REACTIONS The most common adverse reactions (≥25%) in patients with B-cell malignancies (MCL, CLL, WM) were thrombocytopenia* (57%, 52%, 43%), neutropenia* (47%, 51%, 44%), diarrhea (51%, 48%, 37%), anemia* (41%, 36%, 13%), fatigue (41%, 28%, 21%), musculoskeletal pain (37%, 28%†, NA‡), bruising (30%, 12%†, 16%†), nausea (31%, 26%, 21%), upper respiratory tract infection (34%, 16%, 19%), and rash (25%, 24%†, 22%†).

*Based on adverse reactions and/or laboratory measurements (noted as platelets, neutrophils, or hemoglobin

decreased).

† Includes multiple ADR terms.

‡ Not applicable; no associated ADRs.

The most common Grade 3 or 4 non-hematological adverse reactions (≥5%) in MCL patients were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), diarrhea (5%), fatigue (5%), and skin infections (5%). Approximately 6% (CLL), 14% (MCL), and 11% (WM) of patients had a dose reduction due to adverse events. Approximately 5% (CLL), 9% (MCL), and 6% (WM) of patients discontinued due to adverse events. Most frequent adverse events leading to discontinuation were infections, subdural hematomas, and diarrhea in CLL patients and subdural hematoma (1.8%) in MCL patients.

DRUG INTERACTIONS

CYP3A Inhibitors - Avoid co-administration with strong and moderate CYP3A inhibitors. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA® dose.

CYP3A Inducers - Avoid co-administration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment - Avoid use in patients with moderate or severe baseline hepatic impairment. In patients with mild impairment, reduce IMBRUVICA® dose.

Please see full Prescribing Information:

http://www.imbruvica.com/downloads/Prescribing_Information.pdf

About Chronic Lymphocytic Leukemia Chronic Lymphocytic Leukemia (CLL) is a slow-growing blood cancer that most commonly arises from B cells, a type of white blood cell (lymphocyte) that originates in the bone marrow.[3,4] CLL is predominantly a disease of the elderly, with a median age of 71 at diagnosis.[3]

About Janssen Research & Development, LLC At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Janssen Research & Development, LLC; Janssen Products, LP; and Janssen Biotech, Inc. are part of the Janssen

Pharmaceutical Companies of Johnson & Johnson. Please visit **http://www.janssenrnd.com** for more information.

Janssen in Oncology In oncology, our goal is to fundamentally alter the way cancer is understood, diagnosed and managed, reinforcing our commitment to the patients who inspire us. In looking to find innovative ways to address the cancer challenge, our primary efforts focus on several treatment and prevention solutions. These include a focus on hematologic malignancies, prostate cancer and lung cancer; cancer interception with the goal of developing products that interrupt the carcinogenic process; biomarkers that may help guide targeted, individualized use of our therapies; as well as safe and effective identification and treatment of early changes in the tumor microenvironment. Please visit oncology.janssenrnd.com.

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. 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 and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in new product development, including the uncertainty of clinical success and of obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description 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 28, 2014, including in Exhibit 99 thereto, 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

References:

[1] IMBRUVICA Prescribing Information, January 2015 [2] Genetics Home Reference. Isolated growth hormone deficiency. Available at: **http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency**. Accessed May 2015. [3] American Cancer Society. Detailed guide: what is chronic lymphocytic leukemia. Available from: **http://www.cancer.org/acs/groups/cid/documents/webcontent/003111-pdf.pdf**. Accessed May 2015. [4] Shaffer AL, Rosenwald A, Staudt LM. Lymphoid malignancies: the dark side of B-cell differentiation. Nat Rev Immunol. 2002;2(12):920-932.

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