IMBRUVICA® (ibrutinib) Long-term Follow-up Data in Patients Living with Relapsed/Refractory Mantle Cell Lymphoma Show Almost Half Alive at Two Years

December 8, 2014

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- ***Note: This press release corresponds to ASH abstracts 78, 4453 and 4471***

SAN FRANCISCO, CA and RARITAN, NJ, December 8, 2014 - New data presented today at the American Society of Hematology (ASH) Annual Meeting in San Francisco, CA, suggest the current safety and efficacy profile for single-agent IMBRUVICA® (ibrutinib) remained consistent with continued longer-term follow-up in patients living with relapsed/refractory mantle cell lymphoma (MCL), Janssen Research & Development, LLC (Janssen) announced today.

One hundred and eleven patients in the Phase 2 multicenter, open-label, PCYC-1104 study received 560mg IMBRUVICA once daily until disease progression or unacceptable toxicity. IMBRUVICA was associated with a 67 percent investigator-assessed overall response rate (ORR) with a median progression-free survival (PFS) of 13 months. The two-year follow-up data presented at ASH by Michael Wang, M.D., Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center and lead investigator for the pivotal registration trial PCYC-1104, show almost one-third of patients (31 percent) remain progression-free at two years and almost half (47 percent) of the 111 patients in the study remain alive. Additional data were also presented from another IMBRUVICA MCL study (SPARK, MCL2001) around primary resistance observed in patients with relapsed or refractory MCL.

IMBRUVICA is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics, Inc.

"The safety and efficacy over time seen with the use of single-agent IMBRUVICA in people with relapsed or refractory mantle cell lymphoma are very encouraging," said Wang.† "These data further confirm the longer-term potential of IMBRUVICA as a treatment option, directly making a positive impact on our MCL patients."

"The fact that the IMBRUVICA data remain consistent with what was previously seen is extremely positive news," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Head, Janssen. "Other new learnings presented at the meeting add to our breadth of knowledge about the therapy; these include the impact of potential resistance mutations on treatment with IMBRUVICA, as well as its utility in people who have had poor responses to prior treatment, such as chemotherapy."

The PCYC-1104 trial served as the basis for the November 13, 2013 approval of IMBRUVICA in patients with MCL who have received at least one prior therapy. Accelerated approval was granted for this indication based on ORR. Improvements in survival or disease-related symptoms have not been established. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

The most common Grade 3 or greater adverse events (AEs) in the study were infection (28 percent), diarrhea (5 percent) and bleeding (6 percent). Grade 3 or greater AEs occurred in 81 percent of people and serious AEs (SAEs) of any grade occurred in 63 percent of patients. The most frequently reported (occurring in >30 percent of IMBRUVICA patients) AEs of any grade were infection (78 percent), diarrhea (54 percent), bleeding (50 percent), fatigue (49.5 percent), nausea (33 percent) and dyspnea (shortness of breath; 32 percent). Treatment discontinuation due to AEs was reported in 11 percent of patients.

Abstract #4471: IMBRUVICA in MCL Patients Who Progressed after Rituximab-Containing Regimen and Bortezomib
A second poster presented by Wang today reported on data from a Phase 2, multicenter, single-arm study (SPARK) evaluating once-daily IMBRUVICA (560mg) in patients living with relapsed/refractory MCL who had received a rituximab-containing treatment regimen and had progressed after at least two cycles of bortezomib. After a median follow-up of 14.9 months, ORR (the primary endpoint) as assessed by an Independent Review Committee (IRC) was 62.7 percent (95 percent CI, 53.7 percent-71.8 percent) and 20.9 percent achieved a complete response (CR).

Duration of response (DOR), PFS, OS and safety were key secondary endpoints. The majority of people had stage IV disease (77.5 percent) and 76.3 percent of people were considered to be at intermediate or high risk, based on the Mantle Cell Lymphoma International Prognostic Index (MIPI). Patients had received a median of two prior therapies before receiving IMBRUVICA (range 1-8 lines) and nearly half (47.5 percent) had received three or more.

The most common Grade 3 or higher AEs were neutropenia (low neutrophil count; 20.8 percent), thrombocytopenia (low blood platelet count; 13.3 percent) and pneumonia (12.5 percent). The most frequently reported AEs of any grade were fatigue (43.3 percent) and diarrhea (42.5 percent). Hemorrhagic events of any grade were reported in 37.5 percent of patients, including three people (2.5 percent) with major hemorrhagic events. Atrial fibrillation was reported in 13 people (10.8 percent); six patients (5 percent) overall experienced Grade 3 or 4 atrial fibrillation.

Overall, the rate of discontinuation due to AEs was low (6.7 percent), with dose reductions in eight people (6.7 percent). The primary reason for treatment discontinuation was disease progression (44.2 percent).

Abstract #78: Mutational Analysis and Impact on IMBRUVICA Resistance
A separate analysis from the Phase 2 SPARK study in patients with MCL was presented by Sriram Balasubramanian, Ph.D. (Janssen) on Sunday, December 7. Investigators identified a small sub-set of patients who had primary resistance to IMBRUVICA, which was from known and novel mutations. In contrast, almost 60 percent of patients had few or no mutations, which appeared to be associated with a prolonged PFS.

Twenty-five of the 120 people enrolled in the study (22.7 percent) had IRC-confirmed disease progression. These patients had already received a

median of three prior lines of therapy (range 1-5 lines) prior to treatment with IMBRUVICA. After a median treatment duration of 1.54 months, data were collected from 23 of the 25 patients and analyzed for potential genetic mutations. The analysis identified 27 known and novel mutations which may have contributed to patients' primary resistance to IMBRUVICA, including genes involved in NF-kB signaling, as well as the PIM1 and ERBB4 kinases.

About Mantle Cell Lymphoma
Mantle cell lymphoma (MCL) is an aggressive form of blood cancer which arises from B cells, a type of white blood cell (lymphocyte) that originates in the bone marrow. [1,2] MCL is more prevalent in men than women. The majority of patients are in their mid-60s at diagnosis and the median overall survival rate is three to four years.[1,3]

About IMBRUVICA
IMBRUVICA is 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).[4] 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.[4,5] IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.[4] 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. Improvements in survival or disease-related symptoms have not been established. 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

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - 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 anti-platelet or anti-coagulant 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. Twenty-five percent of patients with MCL and 26% of patients with CLL had Grade 3 or greater NCI Common Terminology Criteria for Adverse Events (CTCAE). Monitor patients for fever and infections and evaluate promptly.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 23 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 10%) including 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 8%).

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
MCL: The most common adverse reactions (≥20%) in the clinical trial were thrombocytopenia*, diarrhea (51%), neutropenia*, anemia*, fatigue (41%), musculoskeletal pain (37%), peripheral edema (35%), upper respiratory tract infection (34%), nausea (31%), bruising (30%), dyspnea (27%), constipation (25%), rash (25%), abdominal pain (24%), vomiting (23%), and decreased appetite (21%). *Treatment-emergent decreases (all grades) of platelets (57%), neutrophils (47%) and hemoglobin (41%) were based on laboratory measurements and adverse reactions.

The most common Grade 3 or 4 non-hematological adverse reactions (≥5%) were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), diarrhea (5%), fatigue (5%), and skin infections (5%). Treatment-emergent Grade 3 or 4 cytopenias were reported in 41% of patients.

Ten patients (9%) discontinued treatment due to adverse reactions in the trial (N=111). The most frequent adverse reaction leading to treatment discontinuation was subdural hematoma (1.8%). Adverse reactions leading to dose reduction occurred in 14% of patients.

Fatal and serious cases of renal failure have occurred. Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 9% of patients.

CLL: The most common adverse reactions (≥20%) in the clinical trials were thrombocytopenia (56%), neutropenia (51%), diarrhea (51%), anemia (37%), fatigue (28%), musculoskeletal pain (28%), upper respiratory tract infection (28%), rash (26%), nausea (25%), and pyrexia (24%).

Approximately 5% of patients receiving IMBRUVICA® discontinued treatment due to adverse events. These included infections, subdural hematomas, and diarrhea. Adverse events leading to dose reduction occurred in approximately 6% of patients.

DRUG INTERACTIONS
CYP3A Inhibitors - Avoid concomitant administration with strong or moderate inhibitors of CYP3A. 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 baseline hepatic impairment.

Please see full prescribing information: http://www.imbruvica.com/downloads/Prescribing_Information.pdf

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 and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Please visit http://www.janssenrnd.com for more information.

About Janssen Biotech, Inc.
Janssen Biotech, Inc. redefines the standard of care in immunology, oncology, urology and nephrology. Built upon a rich legacy of innovative firsts, Janssen Biotech has delivered on the promise of new treatments and ways to improve the health of individuals with serious disease. Beyond its innovative medicines, Janssen Biotech is at the forefront of developing education and public policy initiatives to ensure patients and their families, caregivers, advocates and health care professionals have access to the latest treatment information, support services and quality care. For more information on Janssen Biotech, Inc. or its products, visit www.janssenbiotech.com. Follow us on Twitter at www.twitter.com/JanssenUS.

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.

(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, Janssen Biotech, Inc. and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to, challenges inherent in new product development, including obtaining regulatory approvals; financial distress of purchasers of health care products and services; 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 29, 2013, including in Exhibit 99 thereto, and our 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.)

†Disclaimer: Dr. Wang serves as national principal investigator of this Pharmacyclics-sponsored clinical study. He has served as an unpaid advisor to both Pharmacyclics and Janssen in developing the compound ibrutinib. Dr. Wang does not have a financial interest in either company.

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[1] Leukemia and Lymphoma Society. Mantle Cell Lymphoma Facts. http://www.lls.org/content/nationalcontent/resourcecenter/freeeducationmaterials/lymphoma/pdf/mantlecelllymphoma.pdf. Accessed December 2014.

[2] Cancer Research UK. What is mantle cell lymphoma. http://www.cancerresearchuk.org/cancer-help/type/non-hodgkins-lymphoma/about/types/mantle-cell-lymphoma. Accessed December 2014.

[3] Goy A, Bernstein SH, Kahl B, et al. Bortezomib in patients with relapsed or refractory mantle cell lymphoma: updated time-to-event analyses of the multicenter phase 2 PINNACLE study. Ann Oncol. 2009;20:520-525.

[4] IMBRUVICA Prescribing Information, July 2014.

[5] Genetics Home Reference. Isolated growth hormone deficiency. Available from: http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency. Accessed December 2014

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