Media Inquiries:
Satu Kaarina Glawe
Mobile: +49-172-294-6264

Bernadette King
Phone: 1-215-325-2158
Mobile: 1-215-778-3027

Investor Relations:
Lesley Fishman
Phone: 1-732-524-3922

Joseph J. Wolk
Phone: 1-732-524-1142

Medical Information:
Pharmacyclics Medical Information:
1-877-877-3536

Sustained Benefit in Patients with Relapsed/Refractory Mantle Cell Lymphoma Demonstrated by 3½-Year Follow-Up Data of IMBRUVICA® (ibrutinib)

Best outcomes observed in patients treated with IMBRUVICA at first relapse; these patients maintained PFS for a median of nearly three years

This press release corresponds to abstract #151

ATLANTA and RARITAN, NJ, Dec. 9, 2017 – Today, Janssen Research & Development, LLC (Janssen) announced results of a pooled analysis of relapsed/refractory (r/r) mantle cell lymphoma (MCL) patients treated with IMBRUVICA® (ibrutinib). The extended follow-up data demonstrated that patients treated with IMBRUVICA earlier (after first relapse) experienced the best clinical outcomes, in terms of both efficacy and tolerability. These data (abstract #151) were presented in an oral presentation at the 59th American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta.[1] IMBRUVICA, a first-in-class Bruton's tyrosine kinase (BTK) inhibitor, is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.

"Data from this large clinical trial data set with extended follow-up support the early use of ibrutinib in patients with relapsed or refractory mantle cell lymphoma," said Simon Rule, M.D., Professor in Haematology at Plymouth University Medical School, United Kingdom, and lead investigator and presenter of the pooled analysis.* "Long-

term follow-up for ibrutinib demonstrates, that in addition to efficacy, new onset adverse events decrease over time and are generally less common when patients are treated earlier."

MCL is one of several subtypes of B-cell non-Hodgkin's lymphoma (NHL) and represents about six percent (about 4,200) of new cases of NHL each year in the U.S. MCL usually begins with lymph node enlargement and can potentially spread to other tissues such as the bone marrow and liver.[2] Median overall survival for MCL patients is three to four years.[3]

"We are proud to have helped so many patients worldwide in their battle against blood cancers such as mantle cell lymphoma with IMBRUVICA," said Craig Tendler, M.D., Vice President, Late-Stage Development and Global Medical Affairs for Oncology, Janssen Research & Development. "Building on today's oral presentation, we're pleased that the early clinical benefit first seen with IMBRUVICA in patients with relapsed/refractory MCL has been maintained with longer follow-up, and enhanced for those patients treated earlier in their disease course."

Abstract #151: Median 3.5-Year Follow-Up of Ibrutinib Treatment in Patients with Relapsed/Refractory Mantle Cell Lymphoma: A Pooled Analysis
Oral presentation: Saturday, December 9, 2017, 12:00 PM ET

The pooled analysis includes results from Phase 2 and 3 studies (SPARK, PCYC-1104, and RAY; n=370), and additional follow up of 87 patients across these studies who enrolled in the long-term open-label extension study, CAN3001. Eighty-three patients were treated with IMBRUVICA for 3 or more years, and 40 patients were treated with IMBRUVICA for 4 or more years. With 3½ years (41 months) of follow up, the median progression free survival (PFS) overall was 13 months, and 33.6 (range, 19.4-42.1) months in patients with one prior line of therapy. The median PFS in patients achieving complete response (CR) was 46.2 (range, 42.1-not estimable) months and the duration of response in these patients was 55.7 (range, 55.7-NE) months. Patients with favorable baseline disease characteristics were more likely to remain on IMBRUVICA for more than 3 years. Overall, 53% (95% CI, 0.47-0.58), 45% (0.39-0.50), and 37% (0.25-0.49) of patients were alive at 2, 3, and 5 years, respectively, and the median overall survival (OS) was 26.7 months.

Grade 3 or higher treatment-emergent adverse events (TEAEs) occurred in 79.7% of patients, with the new onset events decreasing after the first year. New onset grade 3/4 TEAEs were generally less common in patients who were treated earlier with ibrutinib. In these studies that permitted enrollment of patients with multiple cardiac risk factors, and among patients experiencing grade 3/4 atrial fibrillation, no patients discontinued treatment and <1% had a dose reduction.

About IMBRUVICA
IMBRUVICA® (ibrutinib) was one of the first therapies to receive U.S. approval after having received the FDA's

Breakthrough Therapy Designation. 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] IMBRUVICA targets and blocks BTK, inhibiting the survival and spread of cancer cells, and impacting signaling associated with other serious conditions. Worldwide, IMBRUVICA was used to treat more than 90,000 patients. For more information, visit www.IMBRUVICA.com.

Additional Information about IMBRUVICA®

INDICATIONS

IMBRUVICA® is indicated to treat adults with[5]

- 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 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 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 14% to 29% of patients. 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 (range, 13 to 29%), thrombocytopenia (range, 5 to 17%), and anemia (range, 0 to 13%) based on laboratory measurements occurred in patients with B-cell malignancies treated with single agent 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, hypertension, 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. Atrial fibrillation should be managed appropriately, and if it persists, consider the risks and benefits of IMBRUVICA® treatment and follow dose modification guidelines.

Hypertension: Hypertension (range, 6 to 17%) has occurred in patients treated with IMBRUVICA® with a median time to onset of 4.6 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 (range, 3 to 16%) including non-skin carcinomas (range, 1 to 4%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 2 to 13%).

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 (62%), neutropenia (61%), diarrhea (43%), anemia (41%), musculoskeletal pain (30%), rash (30%), bruising (30%), nausea (29%), fatigue (29%), hemorrhage (22%), and pyrexia (21%).

The most common Grade 3 or 4 adverse reactions (≥5%) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were neutropenia (39%), thrombocytopenia (16%), and pneumonia (10%).

Approximately 6% (CLL/SLL), 14% (MCL), 11% (WM) and 10% (MZL) of patients had a dose reduction due to adverse reactions. Approximately 4%-10% (CLL/SLL), 9% (MCL), and 9 % (WM [6%] 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 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.

DRUG INTERACTIONS

CYP3A Inducers: Avoid coadministration with strong CYP3A inducers.

CYP3A Inhibitors: Dose adjustment may be recommended.

SPECIFIC POPULATIONS

Hepatic Impairment (based on Child-Pugh criteria): Avoid use of IMBRUVICA® in patients with moderate or severe baseline hepatic impairment. In patients with mild impairment, reduce IMBRUVICA® dose.

Please see Full Prescribing Information: https://www.imbruvica.com/prescribing-information.

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 www.janssen.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 www.janssen.com/oncology.

About the Janssen Pharmaceutical Companies

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 www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal.

# # #

**Disclaimer: Dr. Rule served as the lead investigator of this Janssen-sponsored clinical study. Dr. Rule does not have a financial interest in the company.*

[1] Rule, S et al. Median 3.5-year Follow-up of ibrutinib treatment in patients with relapsed/refractory mantle cell lymphoma: a pooled analysis. Oral Presentation at American Society of Hematology Annual Meeting and Exposition 2017; December 2017; Atlanta, GA. Abstract #151.
[2] Leukemia & Lymphoma Society. Mantle cell lymphoma facts. https://www.lls.org/sites/default/files/file_assets/mantlecelllymphoma.pdf. Accessed October 2017.
[3] Herrmann A, Hoster E, Zwingers T, et al. Improvement of overall survival in advanced stage mantle cell lymphoma. *J Clin Oncol*. 2009;27:511–8.
[4] Genetics Home Reference. Isolated growth hormone deficiency. http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency. Accessed April 2017.
[5] Janssen Biotech, Inc., Pharmacyclics LLC. IMBRUVICA U.S. Prescribing Information. August 2017.