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

Investor Relations:
Stan Panasewicz
Phone: 1-732-524-2524

Louise Mehrotra
Phone: 1-732-524-6491

Ibrutinib RESONATE™ Data Show Significant Improvements in Progression-Free Survival and Overall Survival in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

Phase 3 data (Abstract LBA7008) featured in the official press programme of the 50th annual meeting of the American Society of Clinical Oncology and simultaneously published in The New England Journal of Medicine

BEERSE, BELGIUM, May 31, 2014 – Data from the international, multicenter Phase 3 PCYC-1112 (RESONATE™) trial in 391 patients suggest monotherapy ibrutinib administered once-daily significantly lengthened progression-free survival (PFS) (median not reached vs. 8.1 months; HR 0.215, 95% CI, 0.146 to 0.317; P<0.0001) and overall survival (OS) (HR 0.434; 95 CI, 0.238 to 0.789; P=0.0049) versus ofatumumab administered intravenously in patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). Ibrutinib is an investigational compound in the EU within a class of medicines called Bruton's tyrosine kinase (BTK) inhibitors*.

Janssen announced today that the data will be included in a presentation during the official press programme at the American Society of Clinical Oncology (ASCO) meeting in Chicago, IL and simultaneously published in a special edition of *The New England Journal of Medicine.*[1]

*Ibrutinib is defined as an investigational compound as it is not yet approved by any regulatory authority in the EU. On October 30, 2013, Janssen submitted a New Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) for ibrutinib for the treatment of adult patients with relapsed or refractory CLL/SLL or relapsed or refractory mantle cell lymphoma (MCL). Ibrutinib is marketed as IMBRUVICA® in the U.S., where it received approval from the U.S. Food and Drug Administration (FDA) for the treatment of patients with MCL who have received at least one prior therapy[2] and for the treatment of patients with CLL who have received at least one prior therapy.[3]

PFS is the primary endpoint of the RESONATE study, with OS, overall response rate (ORR) and safety as key secondary endpoints. These data will be presented in full by Dr. John C. Byrd, M.D director, Division of Hematology, The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital & Richard J. Solove Research Institute and lead investigator for RESONATE (PCYC-1112) during the oral abstract session on Tuesday, June 3 during the Leukemia, Myelodysplasia, and Transplantation track at 11:57 a.m. CDT.

In 2011, Janssen and Pharmacyclics Inc. entered into an agreement to jointly develop and commercialise ibrutinib.

The results from the RESONATE study showed ibrutinib monotherapy significantly improved PFS, OS and ORR in the difficult-to-treat patient population, regardless of baseline characteristics. The median PFS in the ibrutinib arm was not reached because progression events occurred more slowly than in the ofatumumab arm. The PFS results represent a 79 percent reduction in the risk of progression or death in patients treated with ibrutinib compared to ofatumumab. The OS median was also not reached in either arm because progression events occurred slowly. The OS results represent a 57 percent reduction in the risk of death in patients receiving ibrutinib versus those in the ofatumumab arm.

Additionally, the ORR was significantly higher in patients taking ibrutinib monotherapy versus ofatumumab monotherapy, regardless of response criteria or baseline characteristics. Overall, 43 percent of ibrutinib patients achieved a partial response (PR) compared to only four percent of patients taking ofatumumab ($p<0.0001$), following the International Workshop on CLL (IWCLL) response criteria requiring response to be confirmed for at least two months. An additional 20 percent of ibrutinib treated patients also achieved a PR with lymphocytosis. Investigator-assessed response rates were 85 percent for ibrutinib and 24 percent for patients receiving ofatumumab. Significantly higher response rates were seen in the ibrutinib arm consistently across all baseline sub-groups, including those with a deletion of the short arm of chromosome 17 (del 17p), a genetic mutation typically associated with poor prognoses, or refractory to a purine analogue.

“The phase 3 RESONATE study demonstrated significant progression-free and overall survival benefits in relapsed or refractory CLL patients against the current standard of care,” said Professor Ulrich Jäger, Medical University of Vienna, Department of Medicine, Division of Haematology and Hemostaseology. “The survival improvements seen with use of ibrutinib in this study are particularly encouraging as we

look toward its potential for use in patients with difficult-to-treat disease and may offer physicians an effective single-agent treatment option."

RESONATE is a Phase 3, multi-center, international, open-label, randomised study that examined ibrutinib monotherapy versus ofatumumab monotherapy in relapsed or refractory patients with CLL/SLL who had received at least one prior therapy and were not considered appropriate candidates for treatment with a purine analog (n=391). Patients were administered either 420 mg oral ibrutinib (n=195) once-daily until progression or unacceptable toxicity or intravenous ofatumumab for up to 24 weeks (n=196, initial dose of 300 mg followed by 11 doses at 2,000 mg, per dose and schedule consistent with local labeling).

The primary endpoint of the study was PFS evaluated by an Independent Review Committee (IRC), and key secondary endpoints were OS, ORR and safety. The median follow-up was 9.4 months.

"These data add to the body of clinical data supporting the use of ibrutinib in previously treated CLL patients," said Jane Griffiths, Company Group Chairman of Janssen Europe, the Middle East and Africa (EMEA). "These are the first Phase 3 data for ibrutinib. We're pleased to see the particularly strong hazard ratios for progression-free and overall survival and are encouraged that patients continue to do well on treatment with ibrutinib."

The most common Grade 3 or 4 adverse events (AEs) in the RESONATE trial (occurring in five percent or more of ibrutinib patients) were neutropenia (decreased amount of neutrophils in the blood; 16% in the ibrutinib arm vs. 14% in the ofatumumab arm), pneumonia (7% vs. 5%), thrombocytopenia (decrease in platelets in the blood; 6% vs. 4%) and anaemia (5% vs. 8%). The most commonly occurring side effects (AEs in 20 percent or more of patients) were diarrhea (48% vs.18%), fatigue (28% vs. 30%), pyrexia (fever; 24% vs. 15%), nausea (26% vs.18%), anemia (23% vs. 17%) and neutropenia (21% vs. 15%). Atrial fibrillation of any grade was noted more frequently in patients receiving iburitnib (n=10 patients) versus with ofatumumab (n=1 patient), leading to discontinuation of ibrutinib in one patient.

Treatment discontinuation due to progressive disease were 5% in the ibrutinib arm and 19% in the ofatumumab arm. Treatment discontinuations due to adverse events were low in both study arms, with 4% of patients in both treatment arms (eight patients in the ibrutinib arm and seven patients in the ofatumumab arm). Treatment discontinuation due to death occurred in 4% of patients in the ibrutinib arm

(eight patients) and 5% of patients in the ofatumumab arm (nine patients). These events were most commonly infectious in nature. Total treatment exposure was longer for the ibrutinib arm (approximately 8.6 months, versus 5.3 months on ofatumumab).

In January 2014, RESONATE was stopped early at the unanimous recommendation of an Independent Data Monitoring Committee (IDMC) based on a planned interim analysis which concluded that the study showed a significant difference in PFS as compared to the control (the primary endpoint of the study). The IDMC recommended that the sponsor provide access to ibrutinib to patients in the ofatumumab arm. The data served as the basis of the April 2014 supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) in relapsed or refractory CLL patients who have received at least one prior therapy.

CLL is a slow-growing blood cancer of white blood cells called lymphocytes, most commonly B cells.[4] CLL is the most common adult leukemia in the Western world and predominantly a disease of the elderly with a median age of diagnosis of 72.[4,5] This orphan disease often eventually progresses; patients are faced with fewer treatment options and are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[6] SLL is a slow-growing lymphoma in which too many immature white blood cells cause lymph nodes to become larger than normal.[4]

About Ibrutinib

Ibrutinib is an investigational compound within a class of medicines called Bruton's tyrosine kinase (BTK) inhibitors. BTK is an important protein involved in mediating the cellular signalling pathways which control B cell maturation and survival. In malignant B cells, there is excessive signalling through the B cell receptor signalling (BCR) pathway, which includes BTK. The malignant cell ignores the natural signal to die and continues to develop and proliferate. Malignant cells migrate and adhere to protective environmental areas such as the lymph nodes where they proliferate and survive. Ibrutinib is specifically designed to target and inhibit BTK. Ibrutinib forms a strong covalent bond with BTK, which inhibits the excessive transmission of cell survival signals within the malignant B cells and stops their excessive build up in these protected environmental areas. The efficacy and safety of ibrutinib alone and in combination with other treatments is being studied in several blood cancers including CLL, MCL, Waldenstrom's macroglobulinemia (WM), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and multiple myeloma (MM).[7-11]

Ibrutinib is marketed as IMBRUVICA® in the U.S., where it received approval from the U.S. Food and Drug Administration (FDA) for the treatment of patients with MCL who have received at least one prior therapy on November 13, 2013,[2] followed by further indication approval for the treatment of patients with CLL who have received at least one prior therapy on February 12, 2014.[3] The approval, made ibrutinib one of the first medications to receive FDA approval via the Breakthrough Therapy Designation pathway (a new U.S. FDA mechanism intended to expedite the review and development for new medicines showing great promise to treat serious or life-threatening conditions where there is currently an unmet medical need).

About Janssen

Janssen Pharmaceutical Companies of Johnson and Johnson are dedicated to addressing and solving the most important unmet medical needs of our time, including oncology (e.g. multiple myeloma and prostate cancer), immunology (e.g. psoriasis), neuroscience (e.g. schizophrenia, dementia and pain), infectious disease (e.g. HIV/AIDS, hepatitis C and tuberculosis), and cardiovascular and metabolic diseases (e.g. diabetes). Driven by our commitment to patients, we develop sustainable, integrated healthcare solutions by working side-by-side with healthcare stakeholders, based on partnerships of trust and transparency. More information can be found on www.janssen-emea.com. Follow us on www.twitter.com/janssenEMEA for our latest news.

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 tumour microenvironment.

(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 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 and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges inherent in new product development, including obtaining regulatory approvals; competition, including technological advances, new products and

patents attained by competitors; challenges to patents; changes in behavior and spending patterns or financial distress of purchasers of health care products and services; changes to governmental laws and regulations and domestic and foreign health care reforms; general industry conditions including trends toward health care cost containment; and increased scrutiny of the health care industry by government agencies. 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. Byrd 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. Byrd does not have a financial interest in either company.*

# # #

References

1. Byrd, JC. Ibrutinib versus Ofatumumab in Previously Treated Chronic Lymphoid Leukemia*. NEJM*. 2014. Available from: http://www.nejm.org/. Accessed May 2014.
2. U.S. Food and Drug Administration. Press Announcement: FDA approves Imbruvica for rare blood cancer. Nov 2013. Available from: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm374761.htm. Accessed May 2014.
3. U.S. Food and Drug Administration. Press Announcement: FDA approves Imbruvica to treat chronic lymphocytic leukemia. Feb 2014. Available from: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm385764.htm. Accessed May 2014.
4. American Cancer Society. "Leukemia--Chronic Lymphocytic". Available from: http://www.cancer.org/acs/groups/cid/documents/webcontent/003111-pdf.pdf. Accessed April 2014.
5. Parker, T. Chronic lymphocytic leukemia: prognostic factors and impact on treatment. *Discovery Medicine*. 2011; 57.
6. Veliz M, Pinilla-Ibarz J. Treatment of relapsed or refractory chronic lymphocytic leukemia. *Cancer Control*. 2012 Jan;19(1):37-53.
7. Qiu Y, Kung HJ. Signaling network of the Btk family kinases. *Oncogene* 2000;19:5651-61.
8. Shaffer AL, Rosenwald A, Staudt LM. Lymphoid malignancies: the dark side of B-cell differentiation. *Nat Rev Immunol*. 2002;2:920-32.
9. Puri KD, di Paolo JA, Gold MR. B-cell receptor signaling inhibitors for treatment of autoimmune inflammatory diseases and B-cell malignancies. *Int Rev Immunol* 2013;32:397-427.
10. Woyach JA, Johnson AJ, Byrd JC. The B-cell receptor signaling pathway as a therapeutic target in CLL. *Blood* 2012;120:1175-84.
11. Akinleye A, Chen Y, Mukhi N, Song Y, Liu D. Ibrutinib and novel BTK inhibitors in clinical development. *J Hematol Oncol* 2013;6:59.