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Ibrutinib Three Year Follow-up of Single-Agent and Combination Study Results in Chronic Lymphocytic Leukemia

Oral presentation (Abstract 7014) and poster session (Abstract 7009) featured at the 50th annual meeting of the American Society of Clinical Oncology

BEERSE, BELGIUM, May 31, 2014 – Three year follow-up data from the Phase 1b/2 PCYC-1102 trial of monotherapy ibrutinib showed continued durable responses in patients with treatment-naïve (TN) or relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), according to data from an analysis that will be discussed in an oral presentation on Tuesday, June 3 at the American Society of Clinical Oncology (ASCO) 50th annual meeting in Chicago, IL. Ibrutinib is an investigational compound in the EU within a class of medicines called Bruton's tyrosine kinase (BTK) inhibitors*.

Janssen announced the results today, which show ibrutinib monotherapy continued to produce high overall response rates (ORR) (78 percent for all treated patients, with the median duration of response not achieved after almost 30 months and 25 months for patients with del 17p). Moreover, the rate of Grade 3 or higher adverse events (AEs) and serious adverse events or those leading to hospitalisation decreased after one year on treatment.

*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[1] and for the treatment of patients with CLL who have received at least one prior therapy.[2]

In a separate poster presentation to be discussed today, data suggest the combination of single-agent ibrutinib administered orally once-daily with ofatumumab, a CD20-directed cytolytic monoclonal antibody administered intravenously, is tolerable in patients with previously treated relapsed or refractory CLL/SLL.

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

Three Year Follow-up of Single Agent Ibrutinib in Phase 1b/2 Trial

Three year follow-up from the initial Phase 1b/2 PCYC-1102 trial of single-agent ibrutinib showed continued durable responses in patients with treatment-naïve (TN) (n=31) or relapsed or refractory CLL or SLL (n=101). Ibrutinib was associated with a 78 percent ORR, with durable responses regardless of prior treatment history (83.9 percent in treatment-naïve patients, 76.2 percent in relapsed or refractory patients, 55.9 percent in relapsed or refractory patients with a deletion of the short arm of chromosome 17 [del 17p]). In addition, five patients with relapsed or refractory CLL and two with del 17p achieved a partial response (PR) with lymphocytosis as best response. Patients received either single-agent ibrutinib once-daily at either 420 mg or 840 mg daily. ORR was assessed based on International Working Committee on Chronic Lymphocytic Leukemia (IWCLL) criteria. The median time on study was 29.4 months (range, 0.7-38.1 months).

The median duration of response was not achieved for the full set of patients (n=132) evaluated for the analysis. For relapsed or refractory patients with del 17p, the median duration of response was 25 months (range 4.8-34.3 months).

“These results suggest significantly extended response to ibrutinib in patients with CLL three years after starting treatment,” said Professor Ulrich Jäger, Medical University of Vienna, Department of Medicine, Division of Haematology and Hemostaseology “We are especially encouraged to see that patients showed durable responses to treatment with ibrutinib monotherapy regardless of their treatment history.”

Grade 3 or 4 AEs in the pooled analysis related to ibrutinib (investigator-assessed) decreased from 24 percent to four percent after three years of follow-up. Grade 3 or higher serious AEs (SAEs) related to ibrutinib also decreased over time from eight percent in the first year to one percent after three years of treatment. No new safety signals were observed in long-term follow-up and 64 percent of patients

remain on treatment with ibrutinib. The rate of Grade 3 or higher adverse events or those leading to hospitalization decreased after one year on treatment with ibrutinib.

Combination Data

Separately, data from the Phase 1b/2 PCYC-1109 study, to be presented today at ASCO, showed treatment with monotherapy ibrutinib administered once-daily in combination with ofatumumab administered intravenously is tolerated and highly active in patients with relapsed or refractory CLL/SLL (n=71). The combination produced an 83 percent ORR in patients across all three dosing regimens studied, including a 100 percent ORR (n=27) in patients who started with one cycle of ibrutinib therapy followed by ofatumumab; additionally, two patients in the study achieved a PR with lymphocytosis. Additionally, at 12 months, the average progression-free survival (PFS) across all patients was approximately 88 percent, with 64 percent of patients continuing on monotherapy ibrutinib in a long-term extension study. Three patients with Richter's transformation receiving ibrutinib and ofatumumab achieved disease control followed by progression after Day 471, 168 and 137, respectively.

N=71	**Group 1:** one cycle ibrutinib monotherapy, followed by ofatumumab (n=27)	**Group 2:** ofatumumab on day one/cycle one and ibrutinib on day two/cycle one (n=20)	**Group 3:** two cycles of ofatumumab monotherapy, followed by ibrutinib on day one/cycle three (n=24)
ORR	100%	79%	71%
PFS at 12 months	89%	85%	90%
Median duration of response	Not reached	Not reached	Not reached
Best response	100% (n=23)	84% (n=19)	75% (n=24)

The most common Grade 3 or 4 AE in the study (occurring in 10 percent or more of patients) was neutropenia (17%). The most frequent AEs (occurring in 20 percent or more of patients) were diarrhea (68%), infusion-related reaction (45%), peripheral sensory neuropathy (nerve damage; 42%) and stomatitis (inflammation of the mouth and lips; 37%). Six patients (8%) experienced AEs leading to discontinuation of treatment with ibrutinib. Nine patients (12.7%) died within 30 days of the last dose and two died within the follow-up period.

CLL is a usually slow growing blood cancer that most commonly originates from B cells, a type of white blood cell (lymphocyte) that develops in the bone marrow. B cells are part of the immune system and play an important role in fighting infection in the body. CLL is the most common adult leukemia in the Western world, with the median age at diagnosis being primarily those over 70 years old. The incidence rates among men and women in Europe are approximately 5.87 and 4.01 cases per 100,000 persons per year, respectively. CLL is a chronic disease; median overall survival ranges between 18 months and

more than 10 years according to the stage of disease. When cancer cells are located mostly in the lymph nodes, the disease is called SLL.[3-8]

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).[9-13]

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,[1] followed by further indication approval for the treatment of patients with CLL who have received at least one prior therapy on February 12, 2014.[2] 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.

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(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.)

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