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Ibrutinib Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL) Data Published in The New England Journal of Medicine

A second study in relapsed/refractory mantle cell lymphoma (MCL) also published in the online edition

RARITAN, NJ - June 19, 2013 - Janssen Research & Development, LLC (Janssen) today announced *The New England Journal of Medicine (NEJM)* has published data online about the investigational oral Bruton's Tyrosine Kinase (BTK) inhibitor ibrutinib as a monotherapy in patients with chronic lymphocytic leukemia (CLL). Results from a Phase 1b/2 study show that ibrutinib is well tolerated and produced durable responses at both dose levels studied in patients with relapsed/refractory CLL or small lymphocytic lymphoma (SLL). Promising results were seen in patients with advanced disease and in patients with high risk disease as defined by clinical or genetic features, such as a deletion of part of chromosome 17 (del17p).

A separate study was published in the same online edition, examining the safety and efficacy of ibrutinib for the treatment of relapsed/refractory mantle cell lymphoma (MCL). Ibrutinib is being jointly developed by Janssen and Pharmacyclics, Inc. who also sponsored the studies.

"In the ibrutinib study reported, we continue to observe very promising results in patients with chronic lymphocytic leukemia," said lead author John C. Byrd, M.D., Director, Division of Hematology, and D Warren Brown Professor of Leukemia Research, The Ohio State University, Comprehensive Cancer Center. "The high rate of durable remissions achieved with ibrutinib as a single-agent in relapsed or refractory patients and those at high risk historically appears better than any other single agent tested in CLL."

A subanalysis of the Phase 1b/2 open-label study included 85 patients with relapsed/refractory CLL or SLL, most of whom had advanced disease and were treated with several rounds of different therapies prior to their enrollment. In the study, 35% of patients had del17p. Patients with this chromosomal deletion generally respond poorly to chemotherapy, the current standard of treatment for CLL.

Patients received 420 mg (n=51) or 840 mg (n=34) of ibrutinib monotherapy orally, once daily. Overall response rates were 71% for patients in each treatment arm (dose group). Study patients with a del17p had an overall response rate of 68%. After an estimated median follow-up period of 26 months, 75% of patients were progression free and 83% of patients were still alive.

	420mg (n=51)	840mg (n=34)	High risk del17p within both dosing arms (n=29)
Overall response (%)	71%	71%	68%
Complete response (# of patients)	2	0	1
Partial response (# of patients)	34	24	N/A
Estimated Overall survival (%) at 26 months follow up	83%		
Estimated Progression-free survival (%) at 26 months follow up	75%		

"Among patients with CLL, those with del17p have a particularly poor prognosis. There is a need for new treatment options as the current standard therapy for these patients is inadequate. Recently, ibrutinib was granted a third Breakthrough Therapy Designation by the U.S. FDA for this reason," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Therapeutic Area Head, Janssen. "These data provide important insights into the safety and durability of response of ibrutinib in patients with relapsed and high-risk CLL and SLL."

Most adverse events (AEs) were Grade 1 or 2 in severity, with the most common being diarrhea (47%), infections (33%) and fatigue (28%). Two patients (4%) treated with ibrutinib 420 mg/day and four patients (12%) treated with ibrutinib 840 mg/day experienced an AE leading to treatment discontinuation. The most common grade 3 or greater AEs in both ibrutinib treatment arms were pneumonia (12%) and dehydration (6%), despite the immunocompromised condition of these heavily pretreated patients. Grade 3-4 hematological toxicities were infrequent, with anemia (6%), neutropenia (19%) and thrombocytopenia (6%) as the leading AEs. There was no evidence of cumulative toxicity or long-term safety concerns.

Study Design
The Phase 1b/2, open-label, multicenter study was designed to determine the safety, efficacy, pharmacokinetics and

pharmacodynamics of ibrutinib in patients with relapsed/refractory CLL. The primary objective of the study was to determine the safety of the two fixed-dose regimens of ibrutinib, assessed by evaluating the frequency and severity of AEs. Secondary efficacy endpoints included: overall response rate, progression-free survival and overall survival. The data were presented in part at the annual meeting of the American Society of Hematology in December 2012.

The study enrolled patients with a confirmed diagnosis of relapsed/refractory CLL or SLL (a disease that mirrors the symptoms and progression of CLL) at eight sites in the U.S. Patients who participated in the study had a median of four prior therapies and 65% of the patients had advanced disease. Thirty-five percent of CLL patients had a del17p, a genetic mutation associated with a poor prognosis.

About Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma
CLL is a slow-growing cancer of the white blood cells (lymphocytes), most commonly B-cells. CLL is the most common adult leukemia.[1] The genetic mutation 17p occurs when part of chromosome 17 has been lost. CLL patients with 17p deletion have poor treatment outcomes.[2] 17p deletion is reported in 7% of CLL cases,[3] with approximately 20 to 40% of relapsed/refractory patients harboring the mutation.[4] SLL is a slow-growing lymphoma in which too many immature white blood cells cause lymph nodes to become larger than normal.[5]

About Ibrutinib
Ibrutinib is an investigational, oral Bruton's tyrosine kinase (BTK) inhibitor. The effectiveness and safety of ibrutinib alone or in combination with other treatments is being studied in several B-cell malignancies. Janssen Biotech, Inc. and Pharmacyclics entered a collaboration and license agreement in December 2011 to co-develop and co-commercialize ibrutinib. The regulatory filing for ibrutinib in MCL is expected to be made prior to the end of the third quarter of 2013. Details about the complete ibrutinib clinical program is posted on clinicaltrials.gov.

To date, ibrutinib has been granted three Breakthrough Therapy Designations by the U.S. Food & Drug Administration (FDA) as a monotherapy for the treatment of patients with CLL or SLL with del17p; patients with relapsed/refractory MCL who have received prior therapy, and in patients with Waldenström's macroglobulinemia (WM). The implications of Breakthrough Therapy Designation cannot be determined at this time.

About Janssen Research & Development
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 and Janssen Biotech are part of the Janssen Pharmaceutical Companies. Please visit http://www.janssenrnd.com for more information.

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995. 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 and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to, general industry conditions and competition; economic factors, such as interest rate and currency exchange rate fluctuations; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approvals; 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; 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 Exhibit 99 of Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 30, 2012. Copies of this Form 10-K, as well as subsequent filings, are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertake to update any forward-looking statements as a result of new information or future events or developments.)

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[1] How Common is CLL? Leukemia & Lymphoma Society. http://www.lls.org/#/diseaseinformation/leukemia/chroniclymphocyticleukemia/incidence/. Accessed March 2013.

[2] Non-Hodgkin's Lymphomas. Version 1.2013. NCCN Clinical Practice Guidelines in Oncology. http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf. Accessed March 2013.

[3] Non-Hodgkin's Lymphomas. Version 1.2013. NCCN Clinical Practice Guidelines in Oncology. http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf. Accessed March 2013.

[4] Stilgenbaueer S and Zenz T. Understanding and Managing Ultra High-Risk Chronic Lymphocytic Leukemia. Hematology. 2010: 481-488.

[5] Small Lymphocytic Lymphoma. National Cancer Institute. http://www.cancer.gov/dictionary?cdrid=407751. Accessed March 2013.