



NEWS RELEASE

# Janssen Submits Application to the EMA to Expand Use of IMBRUVICA® (ibrutinib) in Previously Untreated Chronic Lymphocytic Leukaemia Patients

10/30/2015

Janssen Submits Application to the EMA to Expand Use of IMBRUVICA® (ibrutinib) in Previously Untreated Chronic Lymphocytic Leukaemia Patients

BEERSE, BELGIUM, October 30, 2015 - Janssen-Cilag International NV announced today the submission of a Type II variation application to the European Medicines Agency (EMA) seeking to broaden the existing marketing authorisation for IMBRUVICA® (ibrutinib) to include previously untreated patients with chronic lymphocytic leukaemia (CLL). IMBRUVICA is co-developed by Cilag GmbH International, a member of the Janssen Pharmaceutical Companies, and Pharmacyclics LLC, an AbbVie company. Janssen affiliates market IMBRUVICA in EMEA (Europe, Middle East and Africa) as well as the rest of the world, except for the United States, where Janssen Biotech, Inc. and Pharmacyclics LLC co-market it.

The filing is based on data from the randomised, multi-centre, open-label Phase 3 RESONATE™-2 (PCYC-1115) clinical trial assessing the use of IMBRUVICA versus chlorambucil in patients with treatment-naïve CLL or small lymphocytic lymphoma (SLL) aged 65 years or older.

The RESONATE-2 trial, which was sponsored by Pharmacyclics LLC, enrolled 269 patients in the U.S., EU and other regions. Patients were randomised to receive either IMBRUVICA 420 mg orally, once daily until progression or toxicity, or chlorambucil 0.5 to 0.8 mg/kg on days 1 and 15 of each 28-day cycle for up to 12 cycles. At the time of the final analysis the primary endpoint was met, with IMBRUVICA shown to be superior to chlorambucil in terms of progression-free survival (PFS). In addition, IMBRUVICA demonstrated significant improvements in key secondary efficacy endpoints, including overall survival (OS), overall response rate (ORR) and in haematologic function. The safety findings were consistent with previous studies.

The data have been accepted for presentation at an upcoming medical conference and for publication in a peer-reviewed journal. More information about the study can be found on [www.clinicaltrials.gov](http://www.clinicaltrials.gov). On 14 September 2015, Janssen **announced** that a supplemental New Drug Application (sNDA) was filed with the U.S. Food and Drug Administration for treatment-naïve patients with CLL based on these data.<sup>1</sup>

"This submission to expand the use of IMBRUVICA for patients with treatment-naïve CLL is a significant step forward in transforming the treatment journey for these patients," said Jane Griffiths, Company Group Chairman, Janssen Europe, Middle East and Africa. "Our ongoing efforts to further investigate IMBRUVICA in additional populations is part of our commitment to improving outcomes for patients with difficult to manage cancers."

### About IMBRUVICA® (ibrutinib)

IMBRUVICA (ibrutinib) is a first-in-class Bruton's tyrosine kinase (BTK) inhibitor, which works by forming a strong covalent bond with BTK to block the transmission of cell survival signals within the malignant B cells.<sup>2</sup> By blocking this BTK protein, IMBRUVICA helps kill and reduce the number of cancer cells. It also slows down the worsening of the cancer.<sup>3</sup>

IMBRUVICA is currently approved in Europe for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL); adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy, or in first line patients with CLL in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy;<sup>4</sup> and in adult patients with Waldenström's macroglobulinemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.<sup>4</sup> Regulatory approval for additional uses has not yet been granted. Investigational uses for ibrutinib, alone and in combination with other treatments, are under way in several blood cancers including CLL, MCL, WM, diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), multiple myeloma (MM) and marginal zone lymphoma (MZL).

IMBRUVICA is co-developed by Cilag GmbH International, a member of the Janssen Pharmaceutical Companies, and Pharmacyclics LLC, an AbbVie company. Janssen affiliates market IMBRUVICA in EMEA (Europe, Middle East and Africa) as well as the rest of the world, except for the United States, where Janssen Biotech, Inc. and Pharmacyclics LLC co-market it. Janssen and Pharmacyclics LLC are continuing an extensive clinical development programme for IMBRUVICA, including Phase 3 study commitments in multiple patient populations - please see the **IMBRUVICA summary of product characteristics** for further information.

### About CLL

In most patients, CLL is generally a slow-growing blood cancer of the white blood cells called B-lymphocytes.<sup>5</sup> The median age at diagnosis is 72 years,<sup>6</sup> and incidence rates among men and women in Europe are approximately 5.87 and 4.01 cases per 100,000 persons per year, respectively.<sup>7</sup> CLL is a chronic disease; median overall survival ranges

between 18 months and more than 10 years according to the stage of disease.<sup>8</sup> The disease eventually progresses in the majority of patients, and patients are faced with fewer treatment options each time. Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.

CLL cells are found in both the lymphatic system and the blood.<sup>9</sup> When the cancer cells are located mostly in the lymph nodes, the disease is called small lymphocytic lymphoma (SLL). Both CLL and SLL are considered different manifestations of the same entity, as classified in the fourth edition of the World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues.<sup>10</sup>

## 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 haematologic 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, individualised use of our therapies; as well as safe and effective identification and treatment of early changes in the tumour microenvironment.

## About Janssen

Janssen Pharmaceutical Companies of Johnson & 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 diseases (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](http://www.janssen-emea.com). Follow us on [www.twitter.com/janssenEMEA](https://www.twitter.com/janssenEMEA) for our latest news.

Cilag GmbH International; Janssen Biotech, Inc.; and Janssen-Cilag International NV are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

###

## References

Janssen Biotech, Inc. IMBRUVICA® (ibrutinib) Supplemental New Drug Application for Treatment-naive Chronic

Lymphocytic Leukemia Submitted to the U.S. FDA. <http://www.prnewswire.com/news-releases/imbruvica-ibrutinib-supplemental-new-drug-application-for-treatment-naive-chronic-lymphocytic-leukemia-submitted-to-the-us-fda-300142150.html>. Last accessed October 2015.

O'Brien S, Furman RR, Coutre SE, et al. Ibrutinib as initial therapy for elderly patients with chronic lymphocytic leukaemia or small lymphocytic lymphoma: an open-label, multicentre, phase 1b/2 trial. *Lancet Oncol.* 2014;15:48-58.

European Medicines Agency. How is the medicine expected to work? [http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/orphans/2012/06/human\\_orphan\\_001058.jsp&mid=WC0b01ac058001d12b](http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/orphans/2012/06/human_orphan_001058.jsp&mid=WC0b01ac058001d12b). Last accessed October 2015.

Imbruvica Summary of Product Characteristics, September 2015. Available at: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Product\\_Information/human/003791/WC500177775.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003791/WC500177775.pdf). Last accessed October 2015.

American Cancer Society. What is chronic lymphocytic leukemia? Available at: <http://www.cancer.org/cancer/leukemia-chroniclymphocyticcll/detailedguide/leukemia-chronic-lymphocytic-what-is-cll>. Last accessed October 2015.

Eichhorst B, Dreyling M, Robak T, Montserrat E, Hallek M; ESMO Guidelines Working Group. Chronic lymphocytic leukemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2011;22(Suppl.6):vi50-vi54.

Sant M, Allemani C, Tereanu C, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood* 2010;116:3724-34.

Sagatys EM, Zhang L. Clinical and laboratory prognostic indicators in chronic lymphocytic leukemia. *Cancer Control* 2012;19:18-25. Stilgenbauer S, Zenz T. Understanding and Managing Ultra High-Risk Chronic Lymphocytic Leukemia. *Hematology* 2010;481-8.

Hallek M. Signaling the end of chronic lymphocytic leukemia: new frontline. *Blood.* 2013;122:3723-34.

Santos FP, O'Brien S. Small lymphocytic lymphoma and chronic lymphocytic leukemia are they the same disease? *Cancer J.* 2012;8:396-403.

### **Media Enquiries:**

Natalie Buhl

Mobile: +353 (0)85-744-6696

Email: [nbuhl@its.jnj.com](mailto:nbuhl@its.jnj.com)

### **Investor Relations:**

Lesley Fishman

Phone: +1 732-524-3922

Louise Mehrotra

Phone: +1 732-524-6491