European Commission Approves IMBRUVICATM in Two Forms of Blood Cancer

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Beerse / Belgium, 17 October 2014 - Janssen-Cilag International NV (Janssen) announced today that the European Commission has approved IMBRUVICA&™ (ibrutinib) capsules, a first-in-class, once-daily, oral Bruton's tyrosine kinase (BTK) inhibitor. This new approach to treating blood cancers works by blocking BTK, a protein that helps certain cancer cells live and grow.[1] IMBRUVICA is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL), or adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy.[2]

IMBRUVICA is co-developed by Cilag GmbH International (a member of the Janssen Pharmaceutical Companies) and Pharmacyclics Switzerland GmbH. In the European Economic Area, Janssen is the marketing authorisation holder. 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 both companies co-market it.

The decision from the European Commission follows a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) on 24 July 2014.[2] This approval allows for the marketing of IMBRUVICA in all 28 countries of the European Union.

"MCL and CLL with 17p deletion are usually challenging and difficult-to-treat blood cancers that do not respond well to conventional therapies. They usually rapidly progress during or soon after chemotherapy leaving patients with very limited treatment options and poor survival," said Professor Peter Hillmen, Haematology, St. James's University Hospital, Leeds, who is an investigator in the IMBRUVICA CLL clinical trial. "Being able to use IMBRUVICA as a single agent offers a new option and gives renewed hope for physicians and their patients."

CLL in most patients is a slow-growing blood cancer, starting from white blood cells (called lymphocytes) in the bone marrow.[3] The chromosomal abnormalities deletion 17p (del17p) and TP53 mutation are associated with aggressive, treatment-resistant disease.[4] MCL is a rare and aggressive type of B-cell lymphoma that can be challenging to treat and is associated with a poor prognosis.[5,6]

The approval of IMBRUVICA was based on data from the Phase 3 (RESONATE&™ PCYC-1112) and Phase 1b-2 (PCYC-1102) studies in CLL, and the Phase 2 study (PCYC-1104) in MCL.

"We are delighted the European Commission has approved IMBRUVICA as a new treatment approach, which could prolong the lives of patients with these complex blood cancers," said Jane Griffiths, Company Group Chairman, Janssen, Europe, Middle East and Africa (EMEA). "This is a positive step forward for patients, and Janssen is committed to looking into further areas of unmet need in blood cancers where IMBRUVICA could improve outcomes."

NOTES TO EDITORS

CLL Study and Efficacy Results
RESONATE&™ (PCYC-1112) is a Phase 3, multi-centre, international, open-label, randomised study that examined ibrutinib as a single agent (given orally) versus ofatumumab (given intravenously) in relapsed or refractory patients with CLL (n=391).[7]

The results from the study showed that at a median follow up of 9.4 months, single agent ibrutinib significantly improved progression-free survival (PFS), overall survival (OS) and overall response rate (ORR) in this difficult-to-treat patient population, regardless of baseline characteristics [ORR was assessed according to the 2008 International Workshop on CLL (IWCLL) criteria by investigators and an independent review committee (IRC)].[7,8]

The median PFS in the ofatumumab arm was 8.1 months and was not reached in the ibrutinib arm because progression events occurred more slowly. The PFS results represent a 78 percent reduction in the risk of progression or death in patients treated with ibrutinib compared to ofatumumab.7 The OS median was not reached in either arm, but at a median follow up of 9.4 months the results showed a 57 percent reduction in the risk of death in patients receiving ibrutinib versus those receiving ofatumumab. Results were consistent across all baseline sub-groups, including those with del17p.[7]

MCL Study and Efficacy Results
The efficacy of ibrutinib in patients with relapsed or refractory MCL was evaluated in an open-label, multi-centre, single-arm Phase 2 study (PCYC-1104) of 111 treated patients. An overall response rate of 68 percent was observed, with a complete response rate of 21 percent and a partial response rate of 47 percent. With a median follow up of 15.3 months, the median duration of response was 17.5 months; the median progression-free survival was 13.9 months.[9]

CLL and MCL Safety Results
The most commonly occurring adverse reactions (≥ 20 percent) were diarrhoea, musculoskeletal pain, upper respiratory tract infection, bruising, rash, nausea, pyrexia (fever), neutropenia (abnormally low number of white blood cells) and constipation. The most common grade 3/4 adverse reactions (≥ 5 percent) were anaemia, neutropenia, pneumonia and thrombocytopenia (low platelet count).[7,9]

About IMBRUVICA&™
IMBRUVICA (ibrutinib) is a 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.[1] By blocking this BTK protein, IMBRUVICA helps kill and reduce the number of cancer cells. It also slows down the worsening of the cancer.[10]

Investigational uses for ibrutinib, alone and in combination with other treatments, are underway in several blood cancers including CLL, MCL,

Waldenström's macroglobulinemia (WM), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and multiple myeloma (MM); IMBRUVICA is approved for the treatment of CLL and MCL; regulatory approval for additional uses has not yet been granted.

IMBRUVICA received U.S. Food and Drug Administration (FDA) approval for the treatment of patients with MCL in November 2013 and conditional approval for the treatment of CLL in patients who have received at least one prior therapy in February 2014. Regular approval in CLL followed in July 2014, including approval as a first-line therapy in del17p patients. IMBRUVICA is also approved in Israel for the treatment of adult patients with MCL or CLL who have received at least one prior treatment.

About CLL
In most patients, CLL is generally a slow-growing blood cancer of the white blood cells called B-lymphocytes. The median age at diagnosis is 72 years, and incidence rates among men and women in Europe are approximately 5.87 and 4.01 cases per 100,000 persons per year, respectively.[3,11,12]CLL is a chronic disease; median overall survival ranges between 18 months and more than 10 years according to the stage of disease.[13] 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.

Deletion 17p (del17p) and TP53 mutation are associated with aggressive, treatment-resistant disease. The abnormality results in the loss of function of a key gene, TP53. TP53 senses the presence of abnormal DNA and triggers either DNA repair mechanisms or cell death and is important in tumour suppression and the action of cytotoxic chemotherapy.[4] Approximately five to eight percent of patients receiving first-line treatment have del17p at diagnosis. However, incidence of del17p and/or TP53 mutation rises to 29 to 52 percent in patients who have relapsed or refractory disease.[14] The median predicted survival for patients with the del17p mutation or TP53 mutation is just two to three years.11

CLL cells are found in both the lymphatic system and the blood.[15] 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.*[16]

About MCL
MCL is considered a rare disease, characterised by high unmet need and small patient populations impacting fewer than one in 200,000 people in Europe and with a median age at diagnosis of 65.[17,18]MCL is much more predominant in men than women and accounts for three to 10 percent of all non-Hodgkin's lymphomas.[19,20] Median overall survival is typically three to four years, and only one to two years in patients following the first relapse.[18] MCL typically involves the lymph nodes, but can spread to other tissues, such as the bone marrow, liver, spleen and gastrointestinal tract.[21] This challenging disease is associated with poor prognoses.

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 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.

(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 known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, 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 regulations and domestic and foreign health care reforms; and general industry conditions, including trends toward health care cost containment. 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 the company's 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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