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Janssen Receives Positive CHMP Opinion Recommending Expanded Use of Imbruvica®▼(ibrutinib) in Two Indications in Europe

BEERSE, BELGIUM, 28 June 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended broadening the existing marketing authorisation for Imbruvica® (ibrutinib) in two indications. One recommendation is for the use of ibrutinib in combination with obinutuzumab in adult patients with previously untreated chronic lymphocytic leukaemia (CLL).[1] The second is for use of ibrutinib plus rituximab for the treatment of adult patients with Waldenström's macroglobulinemia (WM).[1]

Dr Alessandra Tedeschi, Medical Director, Department of Hematology, Niguarda Hospital, Milan, Italy, and investigator in both the iNNOVATE and iLLUMINATE studies, said: "This is an important step forward in further enhancing our ability as haematologists to meet the treatment needs of more patients with these complex blood cancers. Ibrutinib has already offered important progress in both CLL and WM in the indications for which it is currently approved, and these new combination regimens show the potential to further extend the remission period for patients versus standard of care."

The Positive Opinion for CLL was based on results from the Phase 3 iLLUMINATE (PCYC1130) study, published in *The Lancet Oncology*, which investigated ibrutinib in combination with obinutuzumab versus chlorambucil plus obinutuzumab in patients with newly diagnosed CLL.[2] After a median follow-up of 31.3 months (interquartile range [IQR] 29.4–33.2), median progression-free survival (PFS) was significantly longer in the ibrutinib plus obinutuzumab group (median not reached [95 percent confidence interval [CI] 33.6–non-estimable]) than in the chlorambucil plus obinutuzumab group (19.0 months [15.1–22.1]; hazard ratio 0.23; 95 percent CI 0.15–0.37; p<0.0001).[2]

In WM, the Positive Opinion was supported by data from the Phase 3 iNNOVATE (PCYC-1127) study, presented at the 60th Annual Meeting of the American Society of Hematology (ASH) in December 2018. The study evaluated the safety and efficacy of ibrutinib in combination with rituximab, versus rituximab with placebo, in patients with previously untreated and relapsed/refractory WM.[3] At a median follow up of 30.4 months, a significant improvement in the Independent Review Committee (IRC)-assessed primary endpoint of

PFS was seen with ibrutinib plus rituximab when compared with placebo plus rituximab (estimated 30-month PFS rates were 79 percent vs. 41 percent, respectively).[3]

Additional information about both studies can be found at www.ClinicalTrials.gov (NCT02264574 and NCT02165397).[4,5]

"We are incredibly encouraged by these CHMP recommendations, which represent our continued commitment to develop chemotherapy-free combinations for those living with CLL and WM," said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag France. "Ibrutinib has been used to treat more than 140,000 patients worldwide and we are continuing to deliver on our ambition to optimise outcomes for patients with complex B-cell malignancies, that have in the past been very difficult to treat."

Both Positive Opinions will now be reviewed by the European Commission (EC), which has the authority to grant final approval of the indications.

Ibrutinib, a first-in-class Bruton's tyrosine kinase (BTK) inhibitor, is jointly developed and commercialised by Janssen Biotech, Inc., and Pharmacyclics LLC, an AbbVie company.

Dr Alessandra Tedeschi is co-investigator in both the iNNOVATE and iLLUMINATE studies. She was not compensated for any media work.

#ENDS#

About ibrutinib

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.[6] By blocking this BTK protein, ibrutinib decreases survival and migration of B lymphocytes, thereby delaying progression of the cancer.[7]

Ibrutinib is currently approved in Europe for:[8]

- Chronic lymphocytic leukaemia (CLL): As a single agent for the treatment of adult patients with previously untreated CLL, and as a single agent or in combination with bendamustine and rituximab (BR) for the treatment of adult patients with CLL who have received at least one prior therapy.
- Mantle cell lymphoma (MCL): Adult patients with relapsed or refractory mantle cell lymphoma.
- Waldenström's macroglobulinemia (WM): Adult patients who have received at least one prior therapy or in first-line treatment for patients unsuitable for chemo-immunotherapy.

Ibrutinib is approved in more than 95 countries, and, to date, has been used to treat more than 140,000 patients worldwide across its approved indications.

The most common adverse reactions seen with ibrutinib include diarrhoea, neutropenia, haemorrhage (e.g., bruising), musculoskeletal pain, nausea, rash, and pyrexia.[8]

For a full list of side effects and information on dosage and administration, contraindications and other precautions when using ibrutinib please refer to the Summary of Product Characteristics for further information.

About chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is typically a slow-growing blood cancer of the white blood cells.[9] The overall incidence of CLL in Europe is approximately 4.92 cases per 100,000 persons per year and is about 1.5 times more common in men than in women.[10] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[11]

The disease eventually progresses in the majority of patients, and they are faced with fewer treatment options with each relapse. Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.

About Waldenström's macroglobulinemia

Waldenström's macroglobulinemia (WM) is a rare form of non-Hodgkin's lymphoma (NHL).[12] It causes overproduction of a protein called monoclonal immunoglobulin M (IgM) antibody, which causes a thickening of the blood.[13] Incidence rates among men and women in Europe are approximately 7.3 and 4.2 per million persons, respectively.[14] The causes of WM are unknown, with it typically affecting older adults and being slightly more common in men than women.[12,14]

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen Biotech, Inc. and Janssen-Cilag France are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding a recommendation to broaden the existing marketing authorisation for ibrutinib. 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 materialise, actual results could vary materially from the expectations and projections of Janssen Biotech, Inc., Janssen-Cilag France., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to

applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions 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 30, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, 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 nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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