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Janssen Seeks Expanded Use of IMBRUVICA® (ibrutinib) in Combination with Rituximab for Patients with Previously Untreated Chronic Lymphocytic Leukaemia (CLL)

Application supported by the Phase 3 E1912 study evaluating the use of ibrutinib in combination with rituximab, compared to the chemo-immunotherapy regimen of fludarabine, cyclophosphamide and rituximab (FCR) in patients aged 70 years or younger who have previously untreated CLL

BEERSE, BELGIUM, 20 January 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a Type II variation application to the European Medicines Agency (EMA) seeking to expand the label of IMBRUVICA® (ibrutinib) to include ibrutinib in combination with rituximab for the first-line treatment of patients with chronic lymphocytic leukaemia (CLL).

The submission is supported by data from the Phase 3 E1912 study, designed and conducted in the United States (U.S.) by the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN) and sponsored by the National Cancer Institute (NCI), which is part of the U.S. National Institutes of Health. The study evaluated 529 patients with previously untreated CLL aged 70 years or younger, who were randomly assigned in a 2:1 ratio to receive ibrutinib plus rituximab (n=354) or the chemo-immunotherapy FCR (n=175). The primary endpoint was progression-free survival (PFS) and one of the secondary endpoints was overall survival (OS).[1] The primary study results were previously published in *The New England Journal of Medicine*, and the extended four-year median follow-up results were presented at the 2019 American Society of Hematology (ASH) Annual Meeting.[1,2]

"The ECOG-ACRIN's E1912 study demonstrated that ibrutinib in combination with rituximab has shown superior PFS and OS versus FCR, a chemotherapy-based standard of care for younger patients with newly diagnosed CLL," said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag. "We look forward to working with regulatory authorities to bring ibrutinib to more patients with CLL who may benefit from treatment."

"The E1912 study demonstrated the important clinical benefit of ibrutinib in combination with rituximab in the frontline setting," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Janssen Research & Development, LLC. "We remain committed to replacing long-standing use of chemotherapy with ibrutinib-based combination regimens for the treatment of patients with CLL in the frontline setting."

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About ibrutinib

Ibrutinib is a once-daily, first-in-class Bruton's tyrosine kinase (BTK) inhibitor that is administered orally.[3] Ibrutinib blocks the BTK protein; the BTK protein sends important signals that tell B cells to mature and produce antibodies. BTK signaling is needed by specific cancer cells to multiply and spread.[4] By blocking BTK, ibrutinib may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.[5]

Ibrutinib is currently approved in Europe for:[3]

- Chronic lymphocytic leukaemia (CLL): As a single agent or in combination with obinutuzumab 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): As a single agent for the treatment of adult patients with relapsed or refractory MCL
- Waldenström's macroglobulinemia (WM): As a single agent for the treatment of adult patients who have received at least one prior therapy or in first-line treatment for patients unsuitable for chemo-immunotherapy, and in combination with rituximab for the treatment of adult patients

Ibrutinib is approved in more than 95 countries for at least one indication, and to date, has been used to treat more than 170,000 patients worldwide across its approved indications.[6]

The most common adverse reactions seen with ibrutinib include diarrhoea, neutropenia, haemorrhage (e.g., bruising), musculoskeletal pain, nausea, rash, and pyrexia.[3]

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.[7] 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.[8] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[9]

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 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-Cilag and Janssen Research & Development, LLC 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 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 Research & Development, LLC, 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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