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Media Enquiries:
Noah Reymond
Mobile: +31 621-385-718
Email:
NReymond@ITS.JNJ.com

Investor Relations:
Christopher DelOrefice
Office: +1 732-524-2955

Jennifer McIntyre
Office: +1 732-524-3922

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

Patients who were new to CLL treatment lived longer without disease progression with the IMBRUVICA®-based regimen compared to patients treated with a chemo-immunotherapy regimen[1]

BEERSE, BELGIUM, 07 September 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the European Commission (EC) has approved a variation to the marketing authorisation for IMBRUVICA® (ibrutinib), extending the approved indication in chronic lymphocytic leukaemia (CLL) to include combination with rituximab for previously untreated adult patients. The decision is based on data from the Phase 3 E1912 study that showed previously untreated patients aged 70 years or younger treated with ibrutinib plus rituximab lived longer without disease progression than those treated with the established chemo-immunotherapy regimen fludarabine, cyclophosphamide and rituximab (FCR).[2,3] The study was 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.[2,3]

The study evaluated 529 previously untreated patients with CLL aged 70 years or younger (median age, 58 years) who were randomly assigned to receive six cycles of ibrutinib plus rituximab (IR) (n=354), followed by ibrutinib until disease progression or unacceptable toxicity, or six cycles of FCR (n=175).[2]

At a median follow-up of 37 months, patients treated with IR lived longer without disease progression, with a progression-free survival (PFS) rate of 88 percent, compared to 75 percent for patients treated with FCR (hazard ratio [HR] 0.34; 95% confidence interval [CI], 0.22-0.52; p<0.0001).[1] The study also showed an overall survival (OS) advantage for patients treated with the IR regimen.[1] The primary study results were published previously in *The New England Journal of Medicine*, and with extended 48-month follow-up, as presented at the 2019 American Society of Hematology (ASH) Annual Meeting, the initial treatment benefit is maintained.[2,3]

"Historically, chemotherapy with FCR has been the standard of care, or first treatment prescribed for patients with previously untreated CLL," said John Gribben, MD DSc, Professor of Medical Oncology at St Bartholomew's Hospital, Barts Cancer Institute, Queen Mary, University of London. "This decision by the EC is an important step in being able to offer patients with CLL a non-chemotherapy option in the frontline setting, building on the established efficacy and safety we have come to expect from ibrutinib-based therapy."

"We are delighted with the EC's decision approving the use of ibrutinib in combination with rituximab for these patients," said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag. "This new non-chemotherapy combination regimen can offer extended remission as well as fewer chemotherapy-related side effects for patients living with CLL."

Adverse events for the IR arm were consistent with the known safety profiles for ibrutinib and rituximab.[1] The most common adverse reactions seen with ibrutinib include diarrhoea, neutropaenia, musculoskeletal pain, rash, haemorrhage (e.g., bruising), thrombocytopenia, nausea, pyrexia, arthralgia, and upper respiratory

tract infection.[4] The most common serious adverse reactions (which may affect more than 1 in 20 people) include neutropenia, lymphocytosis, thrombocytopenia, pneumonia, and hypertension.[4]

"Ibrutinib is the most comprehensively studied Bruton's tyrosine kinase (BTK) inhibitor with the longest follow-up across eight positive Phase 3 trials in CLL to date, and is recognised as an important advancement in treatment for patients with CLL," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "This latest milestone highlights our commitment to studying the full potential of ibrutinib and in developing regimens which can transform what a CLL diagnosis means for patients going forward."

This announcement comes after the U.S. Food and Drug Administration's (FDA) approval of this expanded indication for ibrutinib in April 2020.

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About ibrutinib

Ibrutinib is a once-a-day, first-in-class Bruton's tyrosine kinase (BTK) inhibitor that is administered orally.[4] Ibrutinib blocks the BTK protein; the BTK protein sends important signals that tell B cells to mature and produce antibodies. BTK signalling is needed by specific cancer cells to multiply and spread.[5] By blocking BTK, ibrutinib may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.[6]

Indications for which ibrutinib is approved in Europe include:[4]

- Chronic lymphocytic leukaemia (CLL): As a single agent or in combination with rituximab or 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 99 countries for at least one indication, and to date, has been used to treat more than 200,000 patients worldwide.[7]

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.[8] 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.[9] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[10]

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.

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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 29, 2019, 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.

References

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