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News Release

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Phase 3 SHINE Results Show IMBRUVICA® (ibrutinib)-Based Combination Regimen Significantly Reduced the Risk of Disease Progression or Death in Older Patients with Newly Diagnosed Mantle Cell Lymphoma

Primary results from the first frontline Phase 3 study of a Bruton's tyrosine kinase inhibitor in mantle cell lymphoma to be presented as late-breaking data at the 2022 ASCO Annual Meeting and published in The New England Journal of Medicine

BEERSE, BELGIUM, 3 June 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced primary results from the Phase 3 SHINE study (Abstract #7502), which demonstrated that the combination of once-daily oral IMBRUVICA® (ibrutinib) plus bendamustine-rituximab (BR) and rituximab maintenance significantly reduced the risk of disease progression or death by 25 percent compared to patients who received placebo plus BR and rituximab maintenance in patients aged 65 years or older with newly diagnosed mantle cell lymphoma (MCL).[1] This study is one of the largest clinical trials ever conducted in first-line MCL and the first for a Bruton's tyrosine kinase inhibitor (BTKi).[1] The data are being presented in an oral session and featured in a press briefing during the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting, and were published in *The New England Journal of Medicine* today. The data will also be presented as an oral presentation at the 2022 European Hematology Association (EHA) Annual Congress.

MCL is a type of aggressive, rare non-Hodgkin lymphoma (NHL) that is incurable and difficult to treat.[2,3] It commonly affects people over the age of 65, who typically cannot

tolerate intensive chemoimmunotherapy and stem cell transplantation, resulting in poor clinical outcomes and contributing to the need to develop additional treatment options for these patients.[4,5]

"SHINE is a study that looked at first-line treatment of older patients with MCL, who are faced with poor outcomes because they typically cannot tolerate intensive therapy," said Prof. Martin Dreyling,* MD, PhD, Department of Medicine III, LMU Hospital, Munich. "The results demonstrate the potential of this ibrutinib combination as a frontline treatment for patients."

The Phase 3 SHINE (MCL3002) study (NCT01776840) – sponsored by Janssen Biotech, Inc. in collaboration with Pharmacyclics LLC, an AbbVie Company – enrolled 523 patients aged 65 years or older with newly diagnosed MCL.[1] All participants were randomly assigned to receive ibrutinib (560 mg orally daily until progression or unacceptable toxicities) or placebo plus BR for a maximum of six 28-day cycles; participants with a complete response (CR) or partial response (PR) continued to receive maintenance therapy with rituximab every second cycle for a maximum of 12 additional doses.[1] Ibrutinib or placebo was administered daily until progressive disease or unacceptable toxicity.[1]

The SHINE study met its primary endpoint of progression-free survival (PFS). Key findings from the Phase 3 SHINE study include:

- With a median follow-up of 84.7 months, the ibrutinib plus BR and R maintenance combination showed a statistically significant and clinically meaningful 2.3-year improvement in median PFS.[1] Median PFS in the ibrutinib plus BR arm was 6.7 years compared to 4.4 years in the placebo plus BR arm (stratified hazard ratio [HR]: 0.75, 95 percent confidence interval [CI], 0.59-0.96; p = 0.011).[1]
- Key secondary endpoints included: complete response (CR), time-to-next treatment (TTNT), overall survival (OS), and overall response rate (ORR).[1]
    - A CR was achieved in 171 patients (65.5 percent) in the ibrutinib plus BR arm and 151 (57.6 percent) in the placebo plus BR arm (p =0.057).[1] The rates of objective response were similar between the two arms (ibrutinib plus BR: 89.7 percent; placebo plus BR: 88.5 percent).[1]
    - Median TTNT was not reached in the ibrutinib plus BR arm.[1] The median TTNT was 92 months in the placebo plus BR arm (HR: 0.48, 95 percent CI, 0.34-0.66).[1]

- OS was similar between treatment arms and median OS was not reached in either treatment arm (HR: 1.07, 95 percent CI, 0.81-1.40).[1]

"Mantle cell lymphoma is an aggressive blood cancer which can be difficult to treat," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "The data at ASCO are encouraging and support the potential of the addition of targeted therapy to standard therapy in a new, first-line treatment approach that could provide disease control over longer periods of time in these patients."

"Ibrutinib was the first approved Bruton's tyrosine kinase inhibitor and over the past eight years has become a key treatment for MCL and other B-cell malignancies," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Janssen Research & Development, LLC. "The Phase 3 SHINE study reinforces our continued commitment to the development of ibrutinib to provide meaningful differences and change outcomes for patients with B-cell malignancies where high unmet medical needs still remain."

The safety profile of the ibrutinib plus BR regimen was consistent with known safety profiles of ibrutinib as well as BR.[1] Across all treated patients, the most common Grade 3/4 Adverse Events (AEs) ≥5 percent were neutropenia (ibrutinib plus BR: 47.1 percent; BR: 48.1 percent), pneumonia (ibrutinib plus BR: 20.1 percent; BR:14.2 percent), anaemia (ibrutinib plus BR: 15.4 percent; BR: 8.8 percent), thrombocytopenia (ibrutinib plus BR: 12.7 percent; BR: 13.1 percent), rash (ibrutinib plus BR: 12.0 percent; BR: 1.9 percent), and diarrhoea (ibrutinib plus BR: 6.9 percent; BR: 3.8 percent).[1] Treatment-emergent AEs of clinical interest with BTKis included atrial fibrillation which was reported in 13.9 percent of patients in the ibrutinib plus BR arm and 6.5 percent in the placebo arm; hypertension in 13.5 percent and 11.2 percent; major bleeding in 5.8 percent and 4.2 percent; any bleeding 42.9 percent and 21.5 percent; and arthralgia in 17.4 percent and 16.9 percent, respectively.[1]

Ibrutinib is currently approved globally for the treatment of adult patients with MCL who have received at least one prior therapy.[6] On 8th March 2022, Janssen submitted a Type II variation application to the European Medicines Agency (EMA) seeking approval of a new indication for IMBRUVICA® (ibrutinib) in combination with BR for the treatment of adult patients with previously untreated MCL who are unsuitable for autologous stem cell transplantation (ASCT).[7] This filing is supported by the Phase 3 SHINE study.

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About Ibrutinib

Ibrutinib is a once-daily oral medication that is jointly developed and commercialised by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.[6] Ibrutinib blocks the Bruton's tyrosine kinase (BTK) protein, which is needed by normal and abnormal B-cells, including specific cancer cells, to multiply and spread.[8] By blocking BTK, ibrutinib may help move abnormal B cells out of their nourishing environments and inhibits their proliferation.[9]

Ibrutinib is approved in more than 100 countries and has been used to treat more than 250,000 patients worldwide.[10] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[6,11] In October 2021, ibrutinib was added to the World Health Organization's Model Lists of Essential Medicines (EML), which refer to medicines that address global health priorities and which should be available and affordable for all.[12]

Ibrutinib was first approved by the European Commission (EC) in 2014, with indications to date:[6]

- 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.

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 Mantle Cell Lymphoma

Mantle cell lymphoma (MCL) is an aggressive and incurable blood cancer of the white blood cells.[13] It is considered a rare disease, characterised by high unmet need and a small patient population, impacting approximately 0.5 in 100,000 people in the European Union (EU).[14]

MCL is more prevalent in men than women and accounts for 7 to 9 percent of all non-Hodgkin's lymphomas (NHLs) in Europe.[15] It is predominantly a disease of the elderly, with a median age of 65 years at diagnosis.[13]

While patient outcomes have improved in the last few decades,[3] the disease remains difficult to treat and is still characterised by consecutive episodes of disease progression and the need for therapy.[2,16] Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[3,4]

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 & Retina; 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 Pharmaceutica NV, Janssen Biotech, Inc., Janssen-Cilag Limited and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

**Prof. Martin Dreyling, M.D., Ph.D., has been a paid consultant to Janssen; he has not been paid for contributing to this press release.*

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding IMBRUVICA. 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 Research & Development, LLC, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc, 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 behavior 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 January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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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