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News Release

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New IMBRUVICA® (ibrutinib) Data in Fixed-Duration Combination Regimen Presented at EHA 2022 Shows Deep, Durable Response at Three Years in Untreated Chronic Lymphocytic Leukaemia

The all-oral, once-daily combination regimen also demonstrates the potential of immune restoration in this patient population

BEERSE, BELGIUM, 10 June 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new and updated results from the Phase 2 CAPTIVATE study evaluating IMBRUVICA® (ibrutinib) in combination with venetoclax (I+V) as a potential fixed-duration (FD) treatment in adult patients with previously untreated chronic lymphocytic leukaemia (CLL). Updated data from the FD cohort with three years of follow-up show that I+V continues to demonstrate deep and durable responses and clinically meaningful progression free survival (PFS) and overall survival (OS) in the first-line treatment setting.[1] New data will be presented from the minimal residual disease (MRD) cohort, which suggest immune restoration with this combination.[2] These data will be presented during the 2022 European Hematology Association (EHA) Annual Congress taking place in Vienna, Austria June 9-12 (Abstracts #S144 and #P669).

"These promising data highlight the complementary mechanism of action between ibrutinib and venetoclax in a fixed-duration combination regimen," said Carol Moreno, M.D., Ph.D., Consultant Hematologist, Hospital de la Santa Creu Sant Pau, Autonomous University of Barcelona, Barcelona, Spain, and study investigator.[†] "The CAPTIVATE study suggests that

this combination may have the potential to provide treatment-free remissions for patients and effectively eradicate CLL cells and help to restore normal B cells to healthy donor levels in patients with previously untreated CLL who achieve undetectable MRD."

The Phase 2 CAPTIVATE (PCYC-1142) study (NCT02910583) – sponsored by Pharmacyclics LLC, an AbbVie Company, and Janssen Biotech, Inc. – enrolled 323 patients[3] with previously untreated CLL who were younger than 70 years, including patients with high-risk disease, in two cohorts: a FD cohort where all patients stopped therapy after 12 cycles of the combination, regardless of MRD status; and an MRD-guided cohort where treatment duration was guided by the patients' MRD status after 12 cycles of I+V combination (patients who met criteria for confirmed undetectable minimal residual disease (uMRD) were randomized 1:1 to placebo or ibrutinib; patients who did not meet uMRD criteria were randomized to ibrutinib or I+V).[1,2]

"While patient outcomes have improved over the last few decades, unmet needs remain in CLL," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "These data are encouraging and support our commitment to developing innovative and convenient treatment regimens that can help healthcare professionals to better tailor frontline therapy based on patients' individual needs."

Three-Year Follow-Up Data from the FD Cohort of the Phase 2 CAPTIVATE (PCYC-1142) Study of Ibrutinib-Based Combination Regimen in Previously Untreated Patients with CLL (Abstract #P669)[1]

With three years of follow-up data from the FD cohort of CAPTIVATE, I+V continues to demonstrate deep, durable responses and clinically meaningful PFS, including in patients with del(17p)/*TP53* mutated or unmutated immunoglobulin heavy chain gene (IGHV).[1] The clinical data underscore the distinct and complementary modes of action of ibrutinib and venetoclax (a BCL-2 inhibitor).[1] Ibrutinib has been shown to mobilise CLL cells out of lymph nodes and other lymphoid niches[4] into peripheral blood (PB) where they are more susceptible to venetoclax-induced apoptosis, eliminating dividing and resting CLL cells.[1]

Key findings from the Phase 2 CAPTIVATE FD cohort study include:

- At a median follow-up of 38.7 months, the 36-month PFS rate was 88 percent for all treated patients, 80 percent for patients with del(17p)/*TP53* mutated and 86 percent for unmutated IGHV patients (95 percent confidence interval [CI]).[1]

- With three years of follow-up, no additional OS events occurred. The 36-month OS rate was 98 percent, overall (95 percent CI).
    - The 36-month OS rates were similar in patients with del(17p)/*TP53* mutated (96 percent) or unmutated IGHV (97 percent).[1]
- The primary endpoint of complete response (CR) rate was 57 percent (n=159; 95 percent CI, 50-65) and consistent across high-risk subgroups.[1]
- Median duration of CR was not reached (n=91); the 24-month landmark estimate for duration of CR was 94 percent. Median duration of response was not reached for responding patients (n=153).[1]
- Seventy nine percent of patients (n=125) achieved uMRD at any time in the PB and/or bone marrow.[1]
- Of patients with uMRD in peripheral blood at 3 months posttreatment, 78 percent (66/85) of evaluable patients maintained uMRD through 12 months posttreatment.[1]
- All patients are currently off treatment. Frequently occurring treatment-emergent adverse events (TEAEs) (period from first dose until 30 days after the last dose of study treatment) were primarily Grade 1/2 in severity with the exception of neutropenia.[1] Median time to onset of frequently occurring TEAEs generally occurred within four months (87-100 percent).[1] The median time to resolution or improvement ranged from 16.5 days (diarrhoea) to 42.5 days (arthralgia).[1] No new serious adverse events or secondary malignancies have been reported since the primary analysis.[1]
- Twelve patients who progressed after FD treatment with I+V have been retreated with single-agent ibrutinib; 11 of the 12 patients were evaluable for response, with 10 responding.[1]

New Data from the MRD-Guided Cohort of the Phase 2 CAPTIVATE (PCYC-1142) Study of Ibrutinib-Based Combination Regimen Evaluating Immune Restoration in Previously Untreated Patients with CLL (Abstract #S144)[2]

Data on the changes over time in the cellular immune profile in patients with CLL treated with the I+V combination and age-matched healthy donors were featured in an oral presentation at EHA. The I+V combination in the confirmed uMRD placebo arm effectively eradicated CLL cells to healthy donor levels and enabled sustained regeneration of normal B-cell counts.[2]

Immune restoration was evaluated in 79 previously untreated patients with CLL enrolled in the MRD cohort by monitoring changes over time in the cellular immune profile of patients treated with I+V combination regimen and compared to 20 age-matched healthy donors.[2]

Key findings from this analysis include:

- Patients with confirmed uMRD (n=40) had a significantly more pronounced decrease in circulating CLL cell count than patients with uMRD not confirmed (n=39).[2]
    - At Cycles seven and 16 the p-value was <0.0001 with I+V combination therapy.[2]
- From Cycle 16 – 29, patients with confirmed uMRD (n=40) had cell counts similar to those of healthy donors (≤0.8 cell/μL).[2]
- Normalisation of critical immune cells, including T-cell subsets, classical monocytes, and dendritic cell counts was observed in this population.[2]

"These new clinical and immune results from the CAPTIVATE study add further evidence of the potential of ibrutinib in a fixed-duration regimen for previously untreated CLL patients," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Janssen Research & Development, LLC. "Ibrutinib has become a key treatment for CLL, and we continue to explore novel combinations such as I+V which may offer the option of off-treatment, disease-free intervals for patients with B-cell malignancies."

The CAPTIVATE study is part of a comprehensive development program exploring the potential of ibrutinib-based FD therapy. Janssen continues to evaluate the I+V combination regimen and its potential to provide a FD treatment option for people living with CLL. Recently, the *New England Journal of Medicine Evidence* published the primary analysis from the Phase 3 GLOW study, which evaluated the safety and efficacy of the I+V combination in older or unfit patients with CLL, and showed that the combination demonstrated superior PFS and deeper sustained responses compared to chemoimmunotherapy in first-line CLL.[5]

In November 2021, Janssen submitted a Type II variation application to the European Medicines Agency (EMA) seeking approval of a new treatment option for IMBRUVICA® (ibrutinib) as a FD combination with venetoclax (I+V) for adult patients with previously untreated chronic lymphocytic leukaemia (CLL).[6] This filing is supported by the Phase 3 GLOW and Phase 2 CAPTIVATE studies.

#ENDS#

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.[7] 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.[7,11] 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:[7]

- 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.[7]

About Chronic Lymphocytic Leukaemia

Chronic lymphocytic leukaemia (CLL) is typically a slow-growing blood cancer of the white

blood cells.[13] 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.[14] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[15]

While patient outcomes have dramatically improved in the last few decades, the disease is still characterised by consecutive episodes of disease progression and the need for therapy.[16] Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[17]

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.

[†]Dr. Moreno has served as a paid consultant to Janssen; she has not been paid for any media work.

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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