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News Release

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New Data Presented at ASH from the Phase 3 GLOW Study Show Fixed-Duration, First-Line Treatment with IMBRUVICA® (ibrutinib) Plus Venetoclax Demonstrated an Overall Survival Rate of More Than 84 Percent at 54 Months in Patients with Chronic Lymphocytic Leukaemia

Additional data from the Phase 2 CAPTIVATE study, show 82 percent of patients with previously untreated chronic lymphocytic leukaemia (CLL) treated with fixed-duration ibrutinib plus venetoclax did not need next-line treatment at 54 months[1,2]

BEERSE, BELGIUM, 11 December, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new long-term follow-up data at the 2023 American Society of Hematology (ASH) Annual Meeting, from the Phase 3 GLOW (Abstract #634) and Phase 2 CAPTIVATE studies (Abstract #633) evaluating first-line, fixed-duration treatment with IMBRUVICA® (ibrutinib) plus venetoclax (I+V) – both featured as oral presentations at the Congress, taking place in San Diego from 9-12 December.[1,2] The GLOW study demonstrated an estimated 84.5 percent overall survival (OS) rate at 54 months, among older and/or comorbid patients with previously untreated CLL treated with I+V, compared to 63.7 percent for patients treated with chlorambucil plus obinutuzumab (Clb+O).[1]

Phase 2 results from the CAPTIVATE study, which utilised a similar I+V regimen as the GLOW study, showed deep remissions with clinical meaningful progression-free survival (PFS)

with the I+V combination.[2] In the I+V the fixed-duration (FD) cohort, rates of PFS remained high and durable, with 70 percent (95 percent Confidence Interval [CI], 62-77) of patients treated with I+V alive and without disease progression after 54 months.[2]

"We are incredibly proud of the impact ibrutinib continues to have in improving outcomes and experiences for patients living with CLL," said Edmond Chan, MBChB, M.D. (Res), Senior Director, EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "It is the only targeted therapy to demonstrate a significant overall survival benefit in randomised Phase 3 studies in this first-line setting, and the latest updates presented at ASH 2023 show that with longer follow-up, this fixed-duration ibrutinib-based combination regimen maintains deep and durable responses, including in higher-risk patients."

Data on Survival Benefits and Time to Next Treatment for First-Line, Fixed-Duration Treatment with Ibrutinib Plus Venetoclax At Median 57-Month Follow-Up from the GLOW Study

In the GLOW study, patients with CLL aged ≥65 years or 18 to 64 years who also had a cumulative illness rating scale (CIRS) score higher than six or creatine clearance of less than 70 mL/min were randomised to I+V (n=106) or Clb+O (n=105).[1]

"Results from the five-year update of the GLOW study continue to demonstrate the sustained efficacy of fixed-duration I+V in older patients and those with comorbidities with previously untreated CLL," said George Follows, PhD, Consultant Hematologist at Cambridge University Addenbrooks Hospital & Clinical Lead for Lymphoma/CLL.* "While there is currently no cure for CLL, it's very promising to see the consistent efficacy and durable responses from almost five years of follow-up."

Phase 3 GLOW Study Results

- With a median follow-up of 57.3 months (range, 1.7-65.2), the primary endpoint of PFS remained superior for I+V versus Clb+O (HR 0.256 [95% CI, 0.172-0.382]).[1]
    - Estimated PFS rates at 54 months were 66.5 percent in I+V-treated patients compared to 19.5 percent for those treated with Clb+O.[1]
    - Patients treated with I+V continued to have an OS advantage, reducing the risk of death by 55 percent (HR 0.453 [95 percent CI, 0.261-0.785];

p=0.0038).[1] Estimated 54-month OS rates were 84.5 percent in the I+V arm compared to 63.7 percent of patients in the control arm treated with Clb+O.[1]

- The risk of needing second-line therapy was significantly reduced by 82 percent with first-line I+V versus Clb+O (HR 0.185 [95 percent CI, 0.096-0.355]; *p*<0.0001).[1]
    - At 54 months, 87.9 percent of patients treated with I+V did not require subsequent therapy.[1]
- I+V resulted in PFS rates at 54 months for patients with unmutated immunoglobulin heavy-chain variable region gene (uIGHV; n=67) and mutated immunoglobulin heavy-chain variable region gene (mIGHV; n=32) of 59 percent and 90 percent, respectively.[1]
- In patients with mIGHV, PFS rates at 42 months post- I+V treatment were greater than or equal to 91 percent, regardless of minimal residual disease (MRD) status at three months after end of treatment (EOT+3).[1]
- In patients with uIGHV, PFS rates at three years post- I+V treatment were 81 percent for patients achieving uMRD at EOT+3.[1,3]
- Thirty-eight months after the end of I+V treatment, 32.1 percent of patients had undetectable MRD (uMRD).[1] Of the patients who achieved uMRD three months after I+V treatment (n=58), 53.4 percent sustained uMRD status 38 months following treatment.[1,3]
- Results from the four-year follow-up study were recently published in *The Lancet Oncology,* on 6 November, 2023.

Data on Retreatment with Single-Agent Ibrutinib in the Phase 2 CAPTIVATE Study (PCYC-1142)

Phase 2 results from the FD cohort of the CAPTIVATE study, which utilised a similar I+V regimen as the GLOW study in patients with CLL up to 70 years of age, showed deep remissions and clinically meaningful PFS with the I+V combination. Additionally, patients with MRD were evaluated.[2]

Phase 2 CAPTIVATE Study Results

- At nearly five years, 82 percent of patients experienced freedom from next-line CLL treatment (95 percent CI, 76–87).[2]
- Of the 202 patients treated with I+V in either the FD cohort (n=159) or the MRD cohort (n=43), 53 patients have had progressive disease (PD) to date with the majority occurring after two years of completing treatment.[2]

  - Twenty-two of these patients have initiated retreatment with single-agent ibrutinib.[2] With a median follow-up of 17 months (range, 0–45), overall response rate (ORR) in 21 response-evaluable patients was 86 percent, with best response of complete response (CR) (n=1 [5 percent]), partial response (PR; n=17 [81 percent]), PR with lymphocytosis (n=1 [5 percent]), stable disease (n=1 [5 percent]), and PD (n=1 [5 percent]).[2,4]
  - Among these patients there were no ibrutinib dose reductions or discontinuations due to adverse events (AEs) in those retreated with single agent ibrutinib.[2]
- In the FD cohort, the 54-month PFS and OS rates were 70 percent (95 percent CI, 62-77) and 97 percent (95 percent CI, 93-99), respectively.[2]

Updated data for both studies showed the safety profile of the I+V regimen was consistent with known safety profiles of ibrutinib and venetoclax.[2] Safety was not further assessed in the GLOW study as all patients were already past the treatment-emergent period in previous analyses.[1] Safety analysis was limited to the incidence of second primary malignancies.[1] In the CAPTIVATE study, serious AEs considered related to study treatment and second malignancies continued to be collected after completion of fixed-duration treatment.[2] In total, second primary malignancies occurred in eight percent of patients and one AE of basal cell carcinoma occurred during this additional year of follow-up.[2]

"GLOW and CAPTIVATE are the longest fixed-duration I+V studies in patients living with CLL with nearly five years of results," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Johnson & Johnson Innovative Medicine. "Together, the consistency of data from these studies elevate I+V as a first-line, all oral therapy and further demonstrate the long-term scientific innovation of ibrutinib in changing the standard of care for patients living with CLL and other B-cell malignancies."

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About GLOW

The GLOW study (NCT03462719) is a randomised, open-label, Phase 3 trial that evaluated the efficacy and safety of first-line, fixed-duration I+V versus Clb+O in elderly patients (≥65

years of age) with CLL, or patients ages 18-64 with a CIRS score of greater than six or creatinine clearance less than 70 mL/min, who had active disease requiring treatment per the International Workshop on CLL (iwCLL) criteria. Patients with del(17p) or known TP53 mutations were excluded.[1,5] There were 211 patients randomly assigned in a 1:1 ratio to receive either I+V (n=106) and/or Clb+O (n=105) and the median age was 71 years.[5,6] Patients assigned to I+V received treatment for 15 cycles (one cycle is 28 days), starting with three cycles of ibrutinib monotherapy lead-in followed by the combination of I+V for 12 cycles. Patients assigned to Clb+O were treated for six cycles.[5]

Among patients with a partial response or better, MRD in peripheral blood (PB) was evaluated using next-generation sequencing (NGS) via clonoSEQ on-treatment and at 3–6-month intervals post-treatment.[5,6] ClonoSEQ data was used as part of CLL clonal testing.[5,6] The primary endpoint was PFS up to two years and 10 months.[3] Secondary endpoints of the study include OS, MRD negative rate, compete response rate, ORR, duration of response and time-to-next treatment.[5]

About CAPTIVATE

The Phase 2 CAPTIVATE study (NCT02910583) evaluated previously untreated adult patients with CLL who were 70 years or younger, including patients with high-risk disease, in two cohorts: an MRD-guided cohort (n=164; median age, 58 years) and a fixed-duration cohort (n=159; median age, 60 years).[2,7,8] Patients received three cycles of ibrutinib lead-in followed by 12 cycles of I+V (oral ibrutinib [420 mg/d]; oral venetoclax [five-week ramp-up to 400 mg/d]) and the primary endpoint was one-year disease-free survival.[7] In this MRD cohort, after completion of I+V, patients with confirmed uMRD were randomly assigned to double-blind treatment with placebo (i.e., a fixed-duration regimen), or continuous ibrutinib.[7]

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.[9] 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.[10] By blocking BTK, ibrutinib may help move abnormal B-cells out of their nourishing environments and inhibits their proliferation.[11]

Ibrutinib is approved in more than 100 countries and has been used to treat more than 295,000 patients worldwide.[12] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[9,13] In October 2021, ibrutinib was added to the World Health Organization's Model Lists of Essential Medicines (EML), which refers to medicines that address global health priorities and which should be available and affordable for all.[14]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[9]

- As a single agent or in combination with rituximab or obinutuzumab or venetoclax for the treatment of adult patients with previously untreated CLL
- 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
- As a single agent for the treatment of adult patients with relapsed or refractory (RR) mantle cell lymphoma (MCL)
- As a single agent for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy. In combination with rituximab for the treatment of adult patients with WM

For a full list of adverse events 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

CLL is typically a slow-growing blood cancer of the white blood cells.[15] The overall incidence of CLL in Europe is approximately 4.92 cases per 100,000 persons per year and it is about 1.5 times more common in men than in women.[16] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[17]

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.[18] Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[19]

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: Oncology, Immunology, Neuroscience, Cardiovascular, Pulmonary Hypertension, and Retina.

Learn more at www.janssen.com/emea. Follow us at www.linkedin.com/janssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech and Janssen Research & Development, LLC are part of Johnson & Johnson.

** Dr. Follows has provided consulting, advisory, and speaking services to Janssen; he 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 product development and the potential benefits and treatment impact of cilta-cel. 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 Pharmaceutica NV, Janssen-Cilag Limited, Jassen Biotech, Janssen Research and Development, LLC, 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; 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 January 1, 2023, 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 http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. None of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Janssen Research and Development, LLC, 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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