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News Release

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Janssen Receives Positive CHMP Opinion for IMBRUVICA® (ibrutinib) in a Fixed-Duration Combination Regimen for Adult Patients with Previously Untreated Chronic Lymphocytic Leukaemia (CLL)

The positive opinion is based on Phase 3 GLOW and Phase 2 CAPTIVATE study results, which investigated the efficacy and safety of ibrutinib plus venetoclax in patients with previously untreated CLL[1,2]

If approved, this will be the first all-oral, once daily, fixed-duration, combination regimen for first-line treatment of CLL

BEERSE, BELGIUM, 24 June 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion recommending approval of a new treatment option with IMBRUVICA® (ibrutinib) in an oral fixed-duration combination with venetoclax (I+V) for adults with previously untreated chronic lymphocytic leukaemia (CLL).

Outcomes for patients with CLL have improved in the last decade with the advent of oral therapies that target the underlying disease biology.[3] This provides the opportunity to combine these novel treatments for an effective and convenient approach that results in deep responses with time-limited therapy.[1] If approved, I+V will be the first all-oral, once daily, fixed-duration combination treatment with a Bruton's tyrosine kinase (BTK) inhibitor for first-line treatment of patients with CLL.

"With this innovative treatment regimen, healthcare professionals would have the flexibility to use ibrutinib either in a fixed-duration combination or as a continuous therapy, helping

them to better tailor frontline CLL therapy based on patients' individual needs," said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "This recommendation brings us one step closer to European Commission (EC) approval and to providing patients with an all-oral, once daily, fixed-duration regimen, which until this point has not been available with the BTK inhibitor class of treatments."

The CHMP positive opinion is supported by data from the pivotal Phase 3 GLOW study (NCT03462719), which demonstrated that I+V was superior to chlorambucil-obinutuzumab with respect to the primary endpoint, progression-free survival (PFS), in elderly or unfit patients with CLL (PFS hazard ratio [HR]: 0.216; 95 percent confidence interval [CI], 0.131 to 0.357; P<0.001).[1] It is also supported by the fixed-duration cohort of the Phase 2 CAPTIVATE study (NCT02910583) which evaluated I+V in 159 patients with previously untreated CLL who were 70 years or younger, including patients with high-risk CLL disease.[2]

Data from these studies were recently published in *NEJM Evidence*, and *Blood,* respectively,[1,4] and featured as oral presentations at the European Hematology Association (EHA) 2021 Congress. Secondary analyses from GLOW, with additional study follow-up, were presented at the American Society of Hematology (ASH) 2021 Annual Meeting, and additional data from the CAPTIVATE study including clinical outcomes at three years and evidence of immune restoration post-treatment were recently presented at the EHA 2022 Congress.

Updated data for both studies showed the safety profile of the I+V regimen was consistent with known safety profiles of ibrutinib and venetoclax.[1,4] In the GLOW study, the most common treatment-emergent adverse events (TEAEs) were diarrhoea (50.9 percent) and neutropenia (41.5 percent) in the ibrutinib-venetoclax arm, and neutropenia (58.1 percent) and infusion-related reactions (29.5 percent) in the chlorambucil-obinutuzumab arm.[1] TEAEs of Grade 3 or greater occurred in 80 (75.5 percent) and 73 (69.5 percent) of patients in the ibrutinib-venetoclax and chlorambucil-obinutuzumab arms, respectively.[1] In the CAPTIVATE fixed-duration cohort, the most common TEAEs were diarrhoea (62 percent), nausea (43 percent), neutropenia (42 percent), and arthralgia (33 percent) and primarily were Grade 1 or 2 in severity.[4] The most common Grade 3/4 AEs were neutropenia (33 percent), hypertension (6 percent), and decreased neutrophil count (5 percent).[4]

"The promising data from GLOW and CAPTIVATE reinforce the distinct and complementary modes of action between ibrutinib and venetoclax, and the potential of this combination regimen to provide treatment-free remissions for patients," said Craig Tendler, M.D., Global

Head of Late Development, Diagnostics & Medical Affairs, Hematology & Oncology, Janssen Research & Development, LLC. "The positive CHMP opinion for I+V is testament to our commitment and continued leadership in developing innovative and convenient treatment regimens that may help improve outcomes for people living with complex blood cancers like CLL."

#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.[5] 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.[6] By blocking BTK, ibrutinib may help move abnormal B-cells out of their nourishing environments and inhibits their proliferation.[7]

Ibrutinib is approved in more than 100 countries and has been used to treat more than 250,000 patients worldwide.[8] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[5,9] 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.[10]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[5]

- As a single agent or in combination with rituximab or obinutuzumab 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, and in combination with rituximab for the treatment of adult patients with WM

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 the CAPTIVATE study

The Phase 2 CAPTIVATE study 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).[4] Patients in the fixed-duration cohort received 3 cycles of ibrutinib lead-in then 12 cycles of ibrutinib plus venetoclax (oral ibrutinib [420 mg/d]; oral venetoclax [5-week ramp-up to 400 mg/d]) and the primary endpoint was complete response (CR) rate.[4]

About the GLOW study

The Phase 3 GLOW study (N=211; median age, 71 years) is a randomised, open-label trial which evaluated the efficacy and safety of first-line, fixed-duration I+V vs. Clb+O in elderly patients (≥65 years of age) with CLL/SLL, or patients ages 18-64 with a cumulative illness rating scale (CIRS) score of greater than six or creatinine clearance less than 70 mL/min, without del(17p) or known TP53 mutations.[1] Patients in the study were randomised to receive either I+V (n= 106) or Clb+O (n=105).[1]

About Chronic Lymphocytic Leukaemia

Chronic lymphocytic leukaemia (CLL) is typically a slow-growing blood cancer of the white blood cells.[11] 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.[12] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[13]

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.[3] Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[14]

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.

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 (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 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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References

[1] Kater AP, et al. Fixed-Duration Ibrutinib-Venetoclax in Patients with Chronic Lymphocytic Leukemia and Comorbidities. *N Eng J Med Evidence*. 2022.

[2] Ghia P, et al. Fixed-Duration (FD) First-Line Treatment (tx) with Ibrutinib (I) Plus Venetoclax (V) For Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL): Primary Analysis of the FD Cohort of the Phase 2 CAPTIVATE Study. 2021 American Society of Clinical Oncology Annual Meeting. June 4-8, 2021.

[3] Moreno C. Standard treatment approaches for relapsed/refractory chronic lymphocytic leukemia after frontline chemoimmunotherapy. Hematology Am Soc Hematol Educ Program. 2020;2020:33-40.

[4] Tam et al. Fixed-duration ibrutinib plus venetoclax for first-line treatment of CLL: primary analysis of the CAPTIVATE FD cohort. *Blood*. 2022. 139(22):3278–3289.

[5] Imbruvica Summary of Product Characteristics, January 2022. Available at: Imbruvica, INN-ibrutinib (europa.eu). Last accessed: June 2022.

[6] Turetsky A, et al. Single cell imaging of Bruton's tyrosine kinase using an irreversible inhibitor. *Sci Rep*. 2014. 24;4:4782.
[7] de Rooij MF, et al. The clinically active BTK inhibitor PCI-32765 targets B-cell receptor- and chemokine-controlled adhesion and migration in chronic lymphocytic leukemia. *Blood*. 2012. 119(11):2590-2594.
[8] Janssen Data on File (RF-152098). Global number of cumulative patients treated with Ibrutinib since launch. October 2021.
[9] Pollyea DA, et al. A Phase I Dose Escalation Study of the Btk Inhibitor PCI-32765 in Relapsed and Refractory B Cell Non-Hodgkin Lymphoma and Use of a Novel Fluorescent Probe Pharmacodynamic Assay. *Blood*. 2009. 114(22): 3713
[10] World Health Organisation. WHO prioritizes access to diabetes and cancer treatments in new Essential Medicines Lists. Available at: https://www.who.int/news/item/01-10-2021-who-prioritizes-access-to-diabetes-and-cancer-treatments-in-new-essential-medicines-lists. Last accessed: June 2022.
[11] American Cancer Society. What is chronic lymphocytic leukemia? Available at: https://www.cancer.org/cancer/chronic-lymphocytic-leukemia/about/what-is-cll.html. Last accessed: June 2022.
[12] Sant M, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood*. 2010. 116:3724–34.
[13] Eichhorst et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up *Ann Oncol*. 2021. 32(1):23-33.
[14] Molica, S. Current Treatment Options in CLL. *Cancers*. 2021. 13:2468.