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News Release

Media Enquiries:
Jenni Mildon
Mobile: +44 7920 418552
Email: jmildon@its.jnj.com

Investor Relations:
Raychel Kruper
Mobile: +1 732-524-6164
Email: rkruper@its.jnj.com

New Results from the Phase 3 GLOW Study of Fixed-Duration Treatment with IMBRUVICA® (ibrutinib) Plus Venetoclax Demonstrate Robust Efficacy and Sustained Response in Older, Unfit Patients with Previously Untreated Chronic Lymphocytic Leukaemia

With nearly four years of study follow-up, all-oral, fixed-duration IMBRUVICA® (ibrutinib) + venetoclax reduced the risk of progression or death by 79 percent and demonstrated overall survival (OS) advantage versus chemoimmunotherapy[1]

BEERSE, BELGIUM, 10 December 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new four-year follow-up results from the Phase 3 GLOW study (Abstract #93),[1] which showed fixed-duration treatment with IMBRUVICA® (ibrutinib) + venetoclax (I+V) reduced the risk of progression or death by 79 percent among older and/or unfit patients with previously untreated chronic lymphocytic leukaemia (CLL) compared to patients treated with chlorambucil plus obinutuzumab (Clb+O).[1] These results were highlighted in an oral presentation during the 2022 American Society of Hematology (ASH) Annual Meeting, taking place in New Orleans, U.S.[1]

CLL is the most common form of leukaemia in the Western world and currently has no cure.[2,3] While the treatment landscape has evolved significantly since the emergence of targeted agents,[4] there is still significant unmet need for novel treatment options, including fixed-duration regimens.[5]

"The GLOW study results demonstrate the potential of fixed-duration I+V as an additional treatment option for older, unfit patients with CLL in the first-line setting, and this fixed-dose combination may offer a flexible regimen for patients seeking a time-limited treatment approach," said study investigator Carsten Niemann,† M.D., Ph.D., Clinical Associate Professor and Principal Investigator at Rigshospitalet, Copenhagen, Denmark. "This first all-oral, fixed-duration novel combination demonstrates an OS advantage in the first-line treatment of CLL and is an innovative option for patients."

In the study, fixed-duration I+V therapy exhibited robust efficacy in older and/or unfit adults with previously untreated CLL, with a superior and sustained benefit in progression-free survival (PFS) with four years of follow-up.[1] Seventy-five percent of patients treated with the combination were alive and progression-free at 3.5 years.[1] I+V also demonstrated an OS advantage versus Clb+O at this latest study follow-up.[1] Exploratory analyses showed that post-treatment PFS rates were higher for I+V (n=106) than Clb+O (n=105), regardless of minimal residual disease (MRD) status post-treatment.[1]

"In the GLOW study, two highly active blood cancer treatments have been combined in a novel, all-oral, fixed-duration combination to deliver superior progression-free survival and an overall survival advantage versus chlorambucil plus obinutuzumab in the first-line treatment of CLL," said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "These latest results at ASH reinforce our ongoing commitment to developing innovations that not only improve patient outcomes but also provide greater flexibility, so healthcare professionals have the option to tailor ibrutinib-based regimens to best suit patients' needs and preferences."

GLOW Results

- With a median 46 months of follow-up, I+V reduced the risk of disease progression or death by 79 percent versus Clb+O (Hazard Ratio [HR] 0.214; [95 percent Confidence Interval [CI], 0.138 – 0.334]; $p<0.0001$).[1]
- I+V is the first fixed-duration combination to demonstrate an OS advantage compared to Clb+O in the first-line treatment of CLL (HR 0.487; [95 percent CI, 0.262 - 0.907]; nominal $p=0.0205$).[1]
- An estimated 74.6 percent of previously untreated older and/or comorbid patients were alive and progression-free at 3.5 years with I+V treatment compared to an estimated 24.8 percent of patients in the Clb+O cohort.[1]

- PFS at 3.5 years was higher for patients in the I+V arm compared to the Clb+O arm for both unmutated IGHV (uIGHV) and mutated IGHV (mIGHV) CLL.[1]
- PFS was better sustained in the I+V arm compared to the Clb+O arm, regardless of MRD ($\geq 10^{-4}$) status, measured at three months following end of treatment.[1]
- Two years after end of treatment, estimated PFS was ≥ 90 percent for patients with mIGHV CLL, independent of MRD status, and for the 60 percent of patients with uIGHV CLL who achieved uMRD.[1]
    - uIGHV is a key prognostic and predictive factor associated with high-risk CLL that can help to predict disease outcomes and inform treatment choices.[6]

Updated data showed the safety profile of the I+V regimen was consistent with the known safety profiles of ibrutinib and venetoclax.

"Ibrutinib has helped change the standard of care for adults living with CLL and other B-cell malignancies, and this study adds to the extensive body of evidence supporting its potential to provide improved survival for patients with CLL," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Janssen Research & Development, LLC. "At Janssen, we are committed to addressing the unmet needs of patients with CLL through continued investment in our ibrutinib clinical development programme."

In addition to the GLOW results, data from the Phase 2 CAPTIVATE study of the MRD cohort (PCYC-1142) (Abstract #92), which utilised the same I+V schedule for the first 15 cycles as in the GLOW study, were also presented in the same oral session at ASH 2022.[7] After the first 15 cycles, patients with confirmed uMRD (n=86) were randomised to ibrutinib or placebo. Disease-free survival at three years post-randomisation was 93 percent for ibrutinib and 85 percent for placebo. PFS rates at four years from start of treatment were 95 percent and 88 percent, respectively, and OS rates were 98 percent and 100 percent.[7]

During the three-year post-randomisation period in CAPTIVATE, no new atrial fibrillation events occurred in the placebo arm, and no new grade three or higher haemorrhage events occurred in either arm. The incidences of hypertension, arthralgia, neutropenia and diarrhoea were generally infrequent in the placebo arm during this time period.[7] No deaths occurred in either arm during the last 12 months of follow-up.[7]

In August 2022, the European Commission granted marketing authorisation for the expanded use of ibrutinib in combination with venetoclax for adults with previously untreated CLL.[8] The approval is based on the Phase 3 GLOW and Phase 2 CAPTIVATE studies.

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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 aged 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.[9] Patients in the study were randomised to receive either 3 cycles of ibrutinib lead-in, followed by 12 cycles of I+V (n=106), or 6 cycles of Clb+O (n=105).[9]

Among patients with 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 posttreatment.[9] ClonoSEQ data was used as part of CLL clonal testing.[9]

The primary endpoint is PFS assessed by an independent review committee. Secondary endpoints of the study include MRD negative rate, complete response rate, overall response rate, OS, duration of response, and time-to-next treatment.[9]

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).[10] Patients in the MRD cohort received 3 cycles of ibrutinib lead-in followed by 12 cycles of I+V (oral ibrutinib [420 mg/d]; oral venetoclax [5-week ramp-up to 400 mg/d]).[10] Patients who met the stringent random assignment criteria for confirmed undetectable MRD (uMRD) were randomly assigned 1:1 to double-blind placebo or ibrutinib; patients without confirmed uMRD were randomly assigned 1:1 to open-label ibrutinib or ibrutinib plus venetoclax.[10] The primary endpoint was 1-year disease-free survival rate in the confirmed uMRD population.[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.[11] 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.[12] By blocking BTK, ibrutinib may help move abnormal B-cells out of their nourishing environments and inhibits their proliferation.[13]

Ibrutinib is approved in more than 100 countries and has been used to treat more than 270,000 patients worldwide.[14] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[11,15] 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.[16]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[11]

- 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

Chronic lymphocytic leukaemia (CLL) is typically a slow-growing blood cancer of the white blood cells.[17] 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.[18] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[19]

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.[4] Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[20]

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. Niemann has served as a consultant 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 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] Neimann C., et al. Residual Disease Kinetics Among Patients with High-Risk Factors Treated with First-Line Fixed-Duration Ibrutinib plus Venetoclax (Ibr+Ven) versus Chlorambucil plus Obinutuzumab (Clb+O): the GLOW Study. 2022 American Society of Hematology Annual Meeting. December 10, 2022.

[2] Yao Y., et al. The global burden and attributable risk factors of chronic lymphocytic leukemia in 204 countries and territories from 1990 to 2019: analysis based on the global burden of disease study 2019. Biomed Eng Online. 2022; 21: 4.

[3] 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: December 2022.

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

[5] Kater AP, et al. Fixed-Duration Ibrutinib-Venetoclax in Patients with Chronic Lymphocytic Leukemia and Comorbidities. N Eng J Med Evidence. 2022. DOI:https://doi.org/10.1056/EVIDoa2200006.

[6] The Leukemia and Lymphoma Society. Chronic Lymphocytic Leukemia. White Plains, NY: The Leukemia and Lymphoma Society; 2014. Publication No. PS34 40M.

[7] Allen J., et al. Treatment Outcomes After Undetectable MRD With First-Line Ibrutinib (Ibr) Plus Venetoclax (Ven): Fixed Duration Treatment (Placebo) Versus Continued Ibr With Up to 5 Years Median Follow-up in the CAPTIVATE Study. 2022 American Society of Hematology (ASH) Annual Meeting. December 10, 2022.

[8] Janssen.com/emea. European Commission Approves IMBRUVICA® (ibrutinib) in a Fixed-Duration Combination Regimen for Adult Patients with Previously Untreated Chronic Lymphocytic Leukaemia (CLL). Available at: https://www.janssen.com/emea/sites/www_janssen_com_emea/files/emea_glow_ec_approval_release_2022_0.pdf. Last accessed: December 2022.

[9] ClinicalTrials.gov. A Study of the Combination of Ibrutinib Plus Venetoclax Versus Chlorambucil Plus Obinutuzumab for the First-line Treatment of Participants With Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) (GLOW). Available at: https://clinicaltrials.gov/ct2/show/NCT03462719. Last accessed: December 2022.

[10] ClinicalTrials.gov. Ibrutinib Plus Venetoclax in Subjects With Treatment-naive Chronic Lymphocytic Leukemia /Small Lymphocytic Lymphoma (CLL/SLL) (CAPTIVATE). Available at: https://www.clinicaltrials.gov/ct2/show/NCT02910583. Last accessed: December 2022.

[11] Imbruvica Summary of Product Characteristics, November 2022. Available at: https://www.ema.europa.eu/en/documents/product-information/imbruvica-epar-product-information_en.pdf. Last accessed: November 2022.

[12] Turetsky A, et al. Single cell imaging of Bruton's tyrosine kinase using an irreversible inhibitor. Sci Rep. 2014;4:4782.

[13] 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.

[14] Janssen Data on File (RF-241102). Global number of cumulative patients treated with Ibrutinib since launch. June 2022.

[15] 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

[16] 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: December 2022.

[17] 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: December 2022.

[18] Sant M, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. Blood. 2010. 116:3724–34.

[19] Eichhorst B, et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Ann Oncol. 2021 Jan;32(1):23-33.

[20] Bewarder M, et al. Current Treatment Options in CLL. Cancers (Basel). 2021;13(10):2468.

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