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News Release

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New Phase 3 Study Results Show IMBRUVICA® (ibrutinib)-Based Combination Regimen as an All-Oral Fixed-Duration Treatment Demonstrated Superior Progression-Free Survival in Adult Patients with Previously Untreated Chronic Lymphocytic Leukaemia

GLOW study presented as a late-breaking abstract at the European Hematology Association (EHA) Virtual Congress

BEERSE, BELGIUM, 12 June, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced primary results from the pivotal Phase 3 GLOW study (NCT03462719) evaluating fixed-duration IMBRUVICA® (ibrutinib) plus venetoclax (I+V) compared to chlorambucil plus obinutuzumab (Clb+O) for first-line treatment of elderly or unfit patients with chronic lymphocytic leukaemia (CLL).

The study demonstrated superior progression-free survival (PFS) of a once-daily, all-oral, fixed-duration regimen of I+V versus Clb+O as first-line treatment of CLL; the study also showed improved duration of remission and significantly improved depth of remission.[1] With I+V, undetectable minimal residual disease (uMRD) in peripheral blood (PB) was sustained by 85 percent of patients one year after end of treatment.[1] The safety and tolerability profile of I+V was consistent with CLL treatment in an older population with comorbidities.[1] These data were featured in the European Hematology Association (EHA) 2021 Virtual Press Briefing and will be presented as a late-breaking abstract during the EHA Virtual Congress (Abstract #LB1902).

"In the GLOW study, two very active blood cancer treatments are combined to create a complementary therapeutic regimen with the hope that deep responses might enable treatment-free remission for patients," said Arnon Kater*, M.D., Ph.D., deputy head of haematology, University of Amsterdam Faculty of Medicine, the Netherlands and principal study investigator. "The data from GLOW showed that ibrutinib in an oral, once-daily fixed-duration combination with venetoclax outperformed a standard chemoimmunotherapy regimen for older or unfit patients, providing the first comparative evidence that this approach has the potential to improve depth of response and, therefore, extends time to progression versus standard therapy."

The GLOW study evaluated the efficacy and safety of first-line fixed-duration I+V versus Clb+O in elderly patients with CLL, 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.[1] The CIRS score measures comorbidity, or concurrent non-CLL illness, in patients across multiple body systems.[2] GLOW excluded patients with del(17p) or known *TP53* mutations. Randomisation to fixed-duration I+V or a standard six 28-day cycle of Clb+O was stratified by immunoglobulin heavy chain variable region gene (IgHV) mutational status and del(11q) status.[1] Patients in the I+V arm received three cycles of ibrutinib lead-in therapy followed by 12 cycles of combination I+V therapy, and all patients stopped therapy regardless of MRD status.[1] In the study, 106 patients received I+V and 105 received Clb+O (n=211; median age, 71 years).[1]

At a median follow-up of 27.7 months, independent review committee (IRC)-assessed PFS for fixed-duration I+V was superior to Clb+O (Hazard Ratio [HR] 0.216, 95 percent confidence interval [CI], 0.131-0.357; $p < 0.0001$) and the improvement in PFS favouring I+V was consistent across predefined subgroups, including older patients and patients with higher comorbidity scores.[1] Median PFS was not reached for I+V and was 21 months for Clb+O (95 percent CI, 16.6-24.7).[1] At three months after the end of treatment (EOT+3), the rate of uMRD was significantly higher for I+V versus Clb+O in bone marrow (51.9 percent versus 17.1 percent, respectively; $p < 0.0001$) and peripheral blood (54.7 percent versus 39.0 percent, respectively; $p < 0.0001$). Complete response (CR) rates (including complete response with incomplete haematologic recovery) by IRC assessment were also significantly higher for fixed-duration I+V versus Clb+O (38.7 percent vs. 11.4 percent; $p < 0.0001$).[1]

Responses to fixed-duration I+V were sustained after EOT; 84.5 percent (49/58) of patients maintained peripheral blood uMRD from EOT+3 to the assessment 12 months after EOT (EOT+12).[1] Thereby, with a median follow-up of 27.7 months, time to next anti-cancer therapy was extended with I+V vs Clb+O (HR 0.143 [95 percent CI, 0.05-0.41]).[1]

The most common Grade 3 or higher treatment-emergent adverse events (TEAEs) for fixed-duration I+V were neutropaenia/neutrophil count decrease (34.9 percent), infections (17 percent), diarrhoea (10.4 percent); and neutropenia/neutrophil count decrease (49.5 percent), thrombocytopaenia (20 percent), and infections (11.4 percent) for Clb+O.[1] Deaths during treatment occurred in seven patients on fixed-duration I+V and two patients on Clb+O.[1] At time of analysis, overall survival was immature; there were eleven deaths in the fixed-duration I+V arm and twelve in the Clb+O arm.[1]

Data from the Fixed-Duration Cohort of the Phase 2 CAPTIVATE (PCYC-1142) Study of Ibrutinib-Based Combination Regimen in Previously Untreated Patients with CLL (Abstract #S147)

GLOW is part of a comprehensive development programme exploring the potential of ibrutinib-based fixed-duration therapy in previously untreated CLL. This includes the fixed-duration cohort from the Phase 2 CAPTIVATE study in young, fit patients that was recently presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting and will also be presented at EHA (Abstract #S147). The CAPTIVATE study evaluated previously untreated CLL patients 70 years or younger, including patients with high-risk disease.[3] In the fixed-duration cohort (N=159; median age, 60 years), all patients received three cycles of ibrutinib lead-in therapy followed by 12 cycles of combination I+V therapy and then stopped therapy regardless of MRD status.[3] More than 90 percent of patients completed 12 cycles of I+V treatment.[3] At a median follow-up of 27.9 months, the CR rate in the overall population was 56 percent (n=88; 95 percent CI, 48–64) and was consistent across high-risk subgroups.[3] Results also showed that 95 percent of patients treated with fixed-duration I+V were alive and progression-free at two years and deep remissions were seen across all subgroups, including patients with high-risk CLL.[3]

The safety profile of the I+V regimen in CAPTIVATE was consistent with known safety profiles of ibrutinib and venetoclax.[3] Of note, 21 percent of patients were at risk for tumour lysis syndrome (TLS) based on high tumour burden at baseline, and this was reduced to one percent after three cycles of ibrutinib lead-in therapy.[3] Adverse events (AEs) were primarily

Grade 1/2.[3] The most common Grade 3/4 AEs were neutropaenia (33 percent), infections (eight percent), hypertension (six percent), and neutrophil count decrease (five percent).[3] Discontinuations due to AEs were infrequent (three percent for ibrutinib).[3]

"Ibrutinib and venetoclax have complementary mechanisms of action, and the promising results from the CAPTIVATE and GLOW studies show that this all-oral regimen that many patients can take at home may provide an effective, flexible treatment option for patients with CLL seeking a fixed-duration therapy," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "Between these two studies, more than 400 patients across the age and fitness spectrum of CLL patients requiring frontline therapy have been treated with ibrutinib in combination with venetoclax, further demonstrating the potential of ibrutinib in this regimen across multiple patient groups."

"Ibrutinib has been used to treat more than 230,000 patients worldwide and continues to be a mainstay in the treatment of CLL," said Edmond Chan, EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Ltd. "Our goal has always been to lead in innovation, address unmet needs and improve quality of life for patients. This latest data is an encouraging step forward, meaning ibrutinib could be an option both for patients who require continuous treatment as well as those for whom a fixed-duration treatment is most appropriate."

#ENDS#

About Ibrutinib

Ibrutinib is a once-daily, first-in-class Bruton's tyrosine kinase (BTK) inhibitor that is administered orally, and is jointly developed and commercialised by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.[4] Ibrutinib blocks the BTK protein; the BTK protein sends important signals that tell B cells to mature and produce antibodies. BTK signalling is needed by specific cancer cells to multiply and spread.[5] By blocking BTK, ibrutinib may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.[6]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[4]

- 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.

Ibrutinib is approved in more than 100 countries, and, to date, has been used to treat more than 230,000 patients worldwide.[7] Ibrutinib is the only BTKi that has demonstrated overall survival benefits in three CLL clinical trials, with response durability persisting up to 8 years,[8,9,10] and more than seven out of ten patients alive and without disease progression after six and a half years.[9] Ibrutinib has also been shown to mediate short- and long-term immune restoration.[11]

Ibrutinib has been comprehensively studied, with more than 150 active clinical trials in several blood cancers and other serious diseases. 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 Chronic Lymphocytic Leukaemia

Chronic lymphocytic leukaemia (CLL) is typically a slow-growing blood cancer of the white blood cells.[12] 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.[13] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[14]

The disease eventually progresses in the majority of patients, and they are faced with fewer treatment options with each relapse. Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.

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

*Dr. Kater 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. 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 Ltd., 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 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 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent 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 P, et al. Fixed-Duration Ibrutinib Plus Venetoclax (I+V) Versus Chlorambucil Plus Obinutuzumab (Clb+O) for First-Line Treatment of Chronic Lymphocytic Leukemia (CLL): Primary Analysis of the Phase 3 GLOW Study. 2021 European Hematology Association 2021 Virtual Congress. June 9-17, 2021.

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[2] Gribben JG. Chronic lymphocytic leukemia: planning for an aging population. Expert Rev Anticancer Ther. 2010;10(9):1389-1394. doi:10.1586/era.10.127
[3] 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.
[4] Imbruvica Summary of Product Characteristics, January 2021. Available at: https://www.ema.europa.eu/documents/product-information/imbruvica-epar-product-information_en.pdf Last accessed June 2021.
[5] Turetsky, A, et al. Single cell imaging of Bruton's Tyrosine Kinase using an irreversible inhibitor. Scientific Reports. volume 4, Article number: 4782 (2014).
[6] de Rooij MF, Kuil A, Geest CR, 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.
[7] Janssen Data on File (EMEA-SR-2090). Global number of cumulative patients treated with Ibrutinib since launch. May 2021.
[8] Shanafelt TD., et al. Ibrutinib-Rituximab or Chemoimmunotherapy for Chronic Lymphocytic Leukemia. *N Engl J Med.* 2019;381:432-443.
[9] Burger JA., et al. Long-term efficacy and safety of first-line ibrutinib treatment for patients with CLL/SLL: 5 years of follow-up from the phase 3 RESONATE-2 study *Leukemia*. 2020;34:787-798.
[10] Byrd JC., et al. Ibrutinib versus ofatumumab in previously treated chronic lymphoid leukemia. *N Engl J Med.* 2014;371(3):213-223.
[11] Solman IG., et al. Ibrutinib restores immune cell numbers and function in first-line and relapsed/refractory chronic lymphocytic leukemia. *Leuk Res.* 2020;97:106432.
[12] 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 2020.
[13] Sant M, Allemani C, Tereanu C, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood*. 2010; 116:3724–34.
[14] Eichhorst B, Robak T, Montserrat E, et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2015;26(Suppl.5): v78-v84.