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News Release

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New Data from Phase 3 GLOW Study Show Fixed-Duration Treatment with IMBRUVICA® (ibrutinib) Plus Venetoclax Demonstrated Deep and Sustained Undetectable Minimal Residual Disease Outcomes in First-line Chronic Lymphocytic Leukaemia

Updated results from the minimal residual disease (MRD) cohort of the Phase 2 CAPTIVATE study also highlight the potential for treatment-free remissions with ibrutinib plus venetoclax in an oral presentation at ASH 2021[1,2]

BEERSE, BELGIUM, 11 December 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new data from two studies evaluating the efficacy and safety of IMBRUVICA® (ibrutinib) plus venetoclax (I+V) as a potential fixed-duration treatment in adult patients with previously untreated chronic lymphocytic leukaemia (CLL).[1,2] These data were both featured during the American Society of Hematology (ASH) 2021 Annual Meeting. New secondary endpoint data from the Phase 3 GLOW study (NCT03462719) showed that fixed-duration treatment with I+V resulted in undetectable minimal residual disease (uMRD) responses that were deeper compared to patients treated with chlorambucil plus obinutuzumab (Clb+O), and an additional analysis showed that uMRD responses were better sustained during the first year post-treatment.[1]

Updated results from the Phase 2 CAPTIVATE study (NCT02910583) of the same investigational regimen, now with a median 38 months of follow-up, further demonstrated sustained uMRD and disease-free survival (DFS).[2] There were no new MRD relapses, clinical progressions or deaths at 24 months of study follow-up in patients with confirmed uMRD following 12 cycles of combined I+V who were randomised to placebo or continued ibrutinib.[2]

"The data at ASH support the potential of fixed-duration ibrutinib combined with venetoclax in delivering sustained responses in the first-line setting, in a once-daily regimen that is all-oral and chemotherapy-free," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "These data are encouraging, particularly since they include positive outcomes for high-risk patients, as we continue to innovate and work towards providing physicians with new options, most suited to patients' needs and preferences."

Data on MRD Outcomes After Fixed Duration Ibrutinib Plus Venetoclax from the GLOW Study (Abstract #70)

The Phase 3 GLOW study is a randomised, open-label trial which 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 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.[1] Patients in the study were randomised to receive either I+V (n=106) or Clb+O (n=105).[1] Previously reported data were presented at the 2021 European Hematology Association (EHA) Virtual Congress and showed that the study met its primary endpoint of progression-free survival (PFS) as measured by an independent review committee (IRC).[3]

The prespecified secondary endpoint was rate of uMRD (uMRD; $<10^{-4}$), MRD was evaluated via next-generation sequencing (NGS) and reported with cutoffs of $<10^{-4}$ and $<10^{-5}$.[1] Rate of uMRD was reported at three and 12 months after end of treatment in both study arms.[1]

The data presented at ASH demonstrated deeper responses at end of treatment and better sustained uMRD responses during the first year post-treatment with all-oral, once-daily fixed-duration I+V versus Clb+O.[1] Further, responses were proportionally deeper at the

level of $<10^{-5}$ in the I+V arm versus Clb+O arm in both peripheral blood (PB) and bone marrow (BM).[1]

"The GLOW study combines two highly active blood cancer treatments that act by complementary mechanisms to deliver superior progression-free survival versus chlorambucil plus obinutuzumab in the first-line treatment of CLL," said Arnon Kater[†], M.D., Ph.D., Deputy Head of Haematology, Amsterdam University Medical Centres, University of Amsterdam and Chairman of the HOVON CLL Working Group, the Netherlands and principal study investigator. "These latest results from both GLOW and CAPTIVATE show the potential to provide treatment-free remissions for patients through robust disease clearance in lymphoid tissue, blood and bone marrow, and early sustainability of those responses after stopping treatment."

GLOW Results:

- With updated median follow-up of 34.1 months, the 30-month PFS was 80.5 percent with I+V versus 35.8 percent for Clb+O (Hazard ratio [HR] 0.212, 95 percent Confidence Interval [CI], 0.129-0.349; p <0.0001).[1]
- Rates of uMRD $<10^{-5}$ were higher for I+V versus Clb+O in BM (40.6 percent versus 7.6 percent) and in PB (43.4 percent versus 18.1 percent).[1]
    - With I+V, deep responses $<10^{-5}$ were seen in patients with unmutated IGHV CLL, and depth of response was mirrored in PB (49.1 percent) and BM (45.5 percent).[1]
- An additional analysis evaluated sustainability of uMRD response between three and 12 months following end of treatment; 80.4 percent of patients with I+V had sustained uMRD $<10^{-5}$ versus 26.3 percent with Clb+O.[1]
- PFS rate during the first year post-treatment was sustained >90 percent with I+V, independent of BM or PB MRD status at three months after end of treatment.[1]
- Additional follow-up is warranted to confirm the long-term impact of MRD status on PFS.[1]

Data from the MRD Cohort of the Phase 2 CAPTIVATE (PCYC-1142) Study (Abstract #68)

The Phase 2 CAPTIVATE trial evaluated adult patients younger than 70 years, including patients with high-risk disease, in two cohorts: an MRD-guided cohort where treatment duration was guided by the patient's MRD status after 12 cycles of combination I+V

therapy; and a fixed-duration cohort where all patients stopped therapy after 12 cycles of the combination, regardless of MRD status.[2] The primary endpoints of the study included MRD negative response rate, DFS, and complete response rate.[2] Data from the primary analysis from both the fixed-duration and MRD-guided cohorts were previously reported.[4,5] Patients with high-risk disease included unmutated IGHV (60 percent of patients), del(17p)/*TP53* mutation (20 percent), complex karyotype (19 percent), and del(11q) without del(17p) (17 percent).[2] Patients in the MRD-guided cohort (n=164; median age, 58 years) who achieved uMRD [defined as having uMRD ($<10^{-4}$ by 8-colour flow cytometry) serially over at least three cycles and uMRD in both PB and BM with combination therapy], were randomised in a double-blinded fashion to continue treatment with ibrutinib monotherapy or placebo until disease progression.[2] Patients in the MRD-guided cohort who did not achieve uMRD following 12 cycles of combination I+V therapy were randomised to continue ibrutinib monotherapy or the combination.[2]

DFS was defined as freedom from MRD relapse ($\geq 10^{-2}$ confirmed on two separate occasions) and without progressive disease (PD) or death starting from randomisation after 15 cycles of treatment.[2] The two-year DFS rates post-randomisation with time-limited treatment (randomised to placebo) was maintained at 95 percent with an additional year of study follow up.[2] There were no new MRD relapses, disease progressions, or deaths in patients with confirmed uMRD treated with placebo or ibrutinib.[2] Early data suggest that patients who progress after time-limited treatment with I+V have the potential to be successfully retreated with single-agent ibrutinib.[2]

Additionally, the estimated 36-month PFS rates were 95.3 percent with placebo and 100 percent with ibrutinib (95 percent CI, 4.7 percent difference, -1.6–10.9, overall log-rank p=0.1573; placebo 82.7– 98.8, ibrutinib 100-100).[2] Among 12 patients who progressed after fixed-duration treatment, nine patients with available responses all had a partial response to single-agent ibrutinib with limited follow-up; three have pending responses.[2]

With a median study follow-up of 38 months, the safety profile of the I+V regimen in CAPTIVATE was consistent with known safety profiles of ibrutinib and venetoclax.[2] The most common adverse events (AEs) of any Grade 13-24 months post randomisation were arthralgia (29 percent I+V; 22 percent ibrutinib monotherapy) and upper respiratory tract infection (20 percent I+V; 15 percent ibrutinib monotherapy).[2] Grade ≥3 AEs were infrequent across randomised arms with the exception of neutropenia (36 percent).[2]

"GLOW and CAPTIVATE are part of a comprehensive development programme continuing to evaluate the potential of ibrutinib-based therapy in previously untreated CLL patients with various needs and risk factors, including those with high-risk disease," said Craig Tendler, M.D., Global Head of Late Development, Diagnostics & Medical Affairs, Hematology & Oncology, Janssen Research & Development, LLC. "With data from these two studies showing patients can achieve deep responses with this novel ibrutinib plus venetoclax combination, we believe this all-oral, fixed-duration regimen offers patients the potential for treatment-free remissions and physicians the flexibility to use ibrutinib alone or as a combination therapy to meet the different goals and needs of patients."

#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.[6] 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.[7] By blocking BTK, ibrutinib may help move abnormal B-cells out of their nourishing environments and inhibits their proliferation.[8]

Ibrutinib is approved in more than 100 countries and has been used to treat more than 250,000 patients worldwide.[9] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[6,10]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[6]

- 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.

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.[14] 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 Limited 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 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 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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