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News Release

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IMBRUVICA® (ibrutinib)-Based Combination Regimen as a Fixed-Duration, First-Line Treatment for Chronic Lymphocytic Leukaemia Demonstrates High Rates of Disease Control

Janssen presents new data at ASCO showing efficacy of ibrutinib plus venetoclax (CAPTIVATE study) in previously untreated patients with chronic lymphocytic leukaemia, and up to seven-year follow-up results (RESONATE-2 study) on progression-free and overall survival benefits with single-agent ibrutinib

BEERSE, BELGIUM, 19 May, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new data from the fixed-duration cohort of the investigational Phase 2 CAPTIVATE study (PCYC-1142), showing 95 percent of patients treated with fixed duration combined IMBRUVICA® (ibrutinib) plus venetoclax were alive and progression-free at two years.[1] Deep remissions were seen across all subgroups, including patients with high risk chronic lymphocytic leukaemia (CLL).[1] In addition, long-term data from the RESONATE-2 (PCYC-1115/1116) study will be presented, providing the longest follow-up Phase 3 data for any Bruton tyrosine kinase (BTK) inhibitor to date.[2] These data reinforce the long-term survival benefits and well-established safety profile of single-agent ibrutinib for patients with CLL, a type of non-Hodgkin lymphoma and the most common form of leukaemia in adults.[1,2]

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Both studies will be presented during the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, June 4-8, and following at the 26th European Hematology Association (EHA) Congress, June 9-17.

"Ibrutinib was the first BTK inhibitor approved in Europe and has been used to treat more than 230,000 patients worldwide. It is now also the first BTK inhibitor to be studied as a fixed-duration combination treatment option," said Edmond Chan, EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Ltd. "The latest data to be presented at ASCO reinforce the potential of ibrutinib as a foundational treatment option across the CLL landscape and add to the breadth of evidence regarding its efficacy and safety profile."

First Data from the Fixed-Duration Cohort of the Phase 2 CAPTIVATE (PCYC-1142) Study of Ibrutinib-Based Combination Regimen in Previously Untreated CLL Patients (Abstract #7501)[1]

The CAPTIVATE study evaluated previously untreated patients with CLL who were 70 years or younger, including patients with high-risk disease.[1] In the fixed-duration cohort (N=159; median age 60 years), patients received three cycles of ibrutinib lead-in therapy, followed by 12 cycles of combination ibrutinib plus venetoclax therapy, and then stopped therapy regardless of minimal residual disease (MRD) status.[1] More than 90 percent of patients completed planned therapy of ibrutinib plus venetoclax treatment.

At a median follow-up of 27.9 months, the complete response (CR) rate in the overall population was 56 percent (n=88; 95 percent Confidence Interval [CI]: 48–64) and was consistent across high-risk subgroups.[1] Of the patients who achieved a CR, 89 percent had a durable CR of at least one year.[1] Among the remaining 11 percent, one patient had progressive disease; the remaining patients with response follow-up of less than one year were not evaluable.[1] The overall response rate (ORR) was 96 percent.[1] Estimated 24-month progression-free survival (PFS) with ibrutinib plus venetoclax was 93 percent for patients with unmutated IGHV and 97 percent for patients with mutated IGHV (unmutated IGHV 95 percent CI: 85–97; mutated IGHV 95 percent CI: 88–99) and overall survival (OS) was 98 percent (95 percent CI: 94-99) for all treated patients.[1] Seventy-seven and 60 percent of patients achieved undetectable minimal residual disease (uMRD) at any time in the peripheral blood and bone marrow, respectively.[1]

"The use of continuous treatment with ibrutinib in CLL has well been established as the standard of care for patients, including those with high-risk disease," said Paolo Ghia*, M.D., Ph.D., Professor of Medical Oncology, Università Vita-Salute San Raffaele, Italy and principal study investigator. "The latest data from the CAPTIVATE study underscore that ibrutinib in an all-oral fixed duration combination with venetoclax also delivers a high rate of progression-free survival at two years while enabling treatment-free remission for patients."

Of note, 94 percent of patients with high baseline tumour lysis syndrome (TLS) risk based on tumour burden shifted to medium- or low-risk after ibrutinib lead-in therapy, and no TLS events occurred.[1] Adverse events (AEs) were primarily Grade 1/2.[1] The most common Grade 3/4 AEs were neutropaenia (33 percent), infections (eight percent), hypertension (six percent), and neutrophil count decrease (five percent).[1] Discontinuations due to AEs were infrequent (three percent for ibrutinib).[1]

Findings from the uMRD-guided cohort of the CAPTIVATE study were presented at the 2020 American Society of Hematology (ASH) Annual Meeting. The phase 3 GLOW study (NCT03462719) is also evaluating fixed-duration ibrutinib plus venetoclax, with a comparison to chlorambucil plus obinutuzumab, for first-line treatment of younger unfit patients or elderly patients with CLL, regardless of fitness criteria. These studies are part of a comprehensive development programme exploring the potential of ibrutinib-based fixed-duration therapy.

Long-Term Data from the Phase 3 RESONATE-2 Study Demonstrate Efficacy and Safety of Single-Agent Ibrutinib in Previously Untreated CLL Patients (Abstract #7523)[2]

The RESONATE-2 study evaluated 269 previously untreated patients with CLL aged 65 years or older, without del(17p), who were randomly assigned to receive continuous ibrutinib or chlorambucil up to 12 cycles.[2] With up to seven years of follow-up, PFS benefit with single-agent ibrutinib was sustained (PFS Hazard Ratio [HR] 0.160 [95 percent CI: 0.111–0.230]).[2] At 6.5 years, the median PFS with ibrutinib has not been reached; 61 percent of patients treated with single-agent ibrutinib were alive and progression-free compared with nine percent of patients treated with chlorambucil.[2] The PFS benefit for patients treated with ibrutinib was seen in all subgroups, including those with high-risk genomic features of *TP53* mutation, unmutated IGHV or 11q deletion (HR 0.091 [95 percent CI: 0.054–0.152]).[2] Additionally, 78 percent of patients in the ibrutinib treatment-arm were alive at 6.5 years. The CR rate with ibrutinib treatment has increased

over time to 34 percent.[2] Nearly half of patients continue to receive ibrutinib treatment with up to seven years of follow-up.[2]

Single-agent ibrutinib was well tolerated as a long-term treatment with no new safety signals.[2] Ongoing rates of Grade 3 or higher AEs of interest remained low for hypertension (five-to-six-year interval: n=20; six-to-seven-year interval: n=15) and atrial fibrillation (five-to-six-year interval: n=7; six-to-seven-year interval: n=5).[2] Additionally, no Grade 3 or higher major haemorrhage occurred in the five-to-seven-year interval.[2] Any-grade AEs leading to discontinuations were seen in three percent (n=2) of patients from year five to year six and no patients discontinued treatment in the ibrutinib arm due to AEs from year six to year seven.[2]

"The positive results from the CAPTIVATE study demonstrate the potential of ibrutinib and venetoclax, with complementary mechanisms of action, to provide deep responses with a once-daily, fixed-duration combination that can be administered in the outpatient setting for younger, fit patients," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "The results from RESONATE-2 further support the long-term benefit of ibrutinib monotherapy in front line CLL for which the breadth and maturity of data continue to grow in support of this standard-of-care treatment and its impact on progression free and overall survival."

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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.[3] 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.[4] By blocking BTK, ibrutinib may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.[5]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[3]

- 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.[6] Ibrutinib is the only BTKi that has demonstrated overall survival benefits in three CLL clinical trials, with response durability persisting up to 8 years,[7,8,9] and more than seven out of ten patients alive and without disease progression after six and a half years.[2] Ibrutinib is the only BTKi that has been shown to mediate short- and long-term immune restoration.[10]

Ibrutinib is the most comprehensively studied BTKi, 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.[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]

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.

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 Pharmaceutica NV, 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.

* Dr. Paolo Ghia has served as a consultant to Janssen; he has not been paid for any media work.

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