Media Contacts:
Ali Aziz
Phone: (647) 978-2000

Investor Relations:
Raychel Kruper
Phone: (732) 524-6164

Health Canada Authorizes IMBRUVICA® (ibrutinib) in a Fixed-Duration Combination with Venetoclax for Adult Patients with Previously Untreated Chronic Lymphocytic Leukemia (CLL)

All-oral, once-daily, fixed-duration combination regimen authorized for first-line treatment of CLL

Toronto, March 23, 2023/CNW/ – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that Health Canada has issued a Notice of Compliance (NOC) authorizing the expanded use of IMBRUVICA® (ibrutinib) in a first all-oral, fixed-duration (FD) treatment combination with venetoclax (I+V) for adults with previously untreated chronic lymphocytic leukemia (CLL), including those with 17p deletion (del 17p).[1] This authorization is based on the pivotal Phase 3 GLOW study that demonstrated statistically significant improvement in progression-free survival (PFS) in patients treated with I+V versus chlorambucil and obinutuzumab (Clb+O), and the FD cohort of the Phase 2 CAPTIVATE study, which showed deep and durable responses in patients treated with I+V.[1]

In Canada, IMBRUVICA® is currently authorized in several indications across four blood cancers (CLL, mantle cell lymphoma, marginal zone lymphoma and Waldenström's macroglobulinemia).[1] This latest milestone marks the eleventh Health Canada authorization for IMBRUVICA® and is the sixth authorization for IMBRUVICA® in CLL.[1]

"This authorization is significant in providing patients a much-needed additional treatment option that combines the complementary mechanisms of action of both ibrutinib and venetoclax," says Dr. Christine Chen, MMEd, MD, FRCPC, Clinician Investigator, Princess Margaret Cancer Centre. "This combination regimen presents a new therapeutic option through an all oral, fixed duration of I+V for patients with previously untreated CLL, marking a positive shift in how we approach first-line treatment of this disease."

Chronic lymphocytic leukemia is one of the most common types of adult leukemia in Canada,[2] with over 2,200 patients diagnosed each year.[3] Though CLL treatment has advanced significantly in the last decade,[4] an unmet need remains including time-limited combinations of targeted therapies that provide durable remissions and the flexibility to better tailor first-line therapy.[5]

"This milestone reflects Janssen's commitment and dedication to bringing patients new, innovative therapies that support their unmet needs and preferences. Over the years, IMBRUVICA® has helped improve patient outcomes for adults living with CLL and this latest authorization reflects its efficacy and safety as a fixed-duration, combination treatment option in CLL," says Berkeley Vincent, President, Janssen Inc. "We are determined to continue delivering new treatment approaches that change the trajectory of CLL and improve patients' quality of life."

In the pivotal Phase 3 GLOW study, with a median follow-up of 28 months, I+V reduced the risk of disease progression or death by 78 per cent compared with chlorambucil and obinutuzumab.[1] PFS was assessed by an independent review committee, in adult patients with previously untreated active CLL (PFS hazard ratio [HR]: 0.22; 95 per cent confidence interval [CI], 0.13 to 0.36; P<0.0001).[1] The improvement in PFS with I+V was consistent across predefined subgroups, including the high-risk population (TP53 mutation, del11q, or unmutated IGHV) (PFS HR: 0.23; 95 per cent CI, 0.13 to 0.41).[1] The Health Canada authorization is also supported by the Phase 2 CAPTIVATE study which evaluated I+V in patients with previously untreated active CLL who were 70 years or younger.[1] The primary endpoint in the FD cohort, the complete response [CR] rate per investigator assessment, was 55.3 per cent (95 per cent CI, 47.6 to 63.1) for all patients.[1] For patients without del 17p mutation in the FD cohort, the complete response rate per investigator assessment was 55.9 per cent; 95 per cent CI: 47.5, 64.2.[1]

In GLOW, adverse reactions reflect exposure to I+V with a median duration of 13.8 months and exposure to Clb+O with a median duration of 5.1 months.[1] The most common adverse reactions (all grades) were diarrhea (51 per cent) and neutropenia (42 per cent) in the I+V arm, and neutropenia (59 per cent) and thrombocytopenia (28 per cent) in the Clb+O arm.[1] The most common adverse reactions greater or equal to grade 3 in GLOW were neutropenia (35 per cent), diarrhea (10 per cent), pneumonia (9 per cent), hypertension (9 per cent) in the I+V arm, and neutropenia (51 per cent), thrombocytopenia (21 per cent) and pneumonia (6 per cent) in the Clb+O arm.[1] In CAPTIVATE, with a median duration of exposure to I+V of 14.1 months, the most common adverse reactions (all grades) were diarrhea (67 per cent), neutropenia (48 per cent), bruising (47 per cent), nausea (44 per cent) and musculoskeletal pain (41 per cent).[1] The most common adverse reactions greater or equal to grade 3 in CAPTIVATE were neutropenia (38 per cent), hypertension (7 per cent), thrombocytopenia (4 per cent), and diarrhea (4 per cent).[1]

About IMBRUVICA®

IMBRUVICA® is co-developed by Cilag GmbH International (a member of the Janssen Pharmaceutical Companies) and Pharmacyclics LLC, an AbbVie company. Janssen Inc. commercializes IMBRUVICA® in Canada. IMBRUVICA® 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, IMBRUVICA® may help move abnormal B-cells out of their nourishing environments and inhibit their proliferation.[7] The distinct and complementary modes of action of I+V target specific cell compartments and CLL cell subpopulations to eliminate both dividing and resting CLL cells.[1] IMBRUVICA® mobilizes CLL cells out of lymph nodes as well as enhances their dependence on BCL-2 making them more susceptible to venetoclax-induced cell death.[1]

IMBRUVICA® was first authorized by Health Canada in 2014, and authorized indications to date include:[1]

- As a single agent for the treatment of adult patients with previously untreated CLL, including those with 17p deletion.
- In combination with obinutuzumab for the treatment of adult patients with previously untreated CLL, including those with 17p deletion.
- In combination with rituximab for the treatment of adult patients with previously untreated CLL.
- In combination with venetoclax for the treatment of adult patients with previously untreated CLL, including those with 17p deletion.
- As a single agent for the treatment of adult patients with CLL who have received at least one prior therapy, including those with 17p deletion.
- In combination with bendamustine and rituximab for the treatment of adult patients with CLL who have received at least one prior therapy.
- As single agent for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).
- As a single agent for the treatment of adult patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy.
- As a single agent for the treatment of adult patients with Waldenström's macroglobulinemia (WM).
- In combination with rituximab for the treatment of adult patients with WM.
- As a single agent for the treatment of adult patients with steroid dependent or refractory chronic graft versus host disease (cGVHD).

About the GLOW study
GLOW is a randomized, open-label, Phase 3 study of IMBRUVICA® in combination with venetoclax versus chlorambucil in combination with obinutuzumab, conducted in patients with previously untreated active CLL who were 65 years or older, and adult patients <65 years of age with a cumulative illness rating scale (CIRS) score >6 or CrCL ≥30 to <70 mL/min, including 14 patients with clinical presentation of SLL.[1] Patients with del 17p or known TP53 mutations were excluded.[1] Patients (n=211) were randomized 1:1 to receive either IMBRUVICA® in combination with venetoclax or chlorambucil in combination with obinutuzumab.[1] Patients in the study were randomized 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).[1] The primary endpoint was progression-free survival (PFS) assessed by an independent review committee.[1]

About the CAPTIVATE study
CAPTIVATE is a Phase 2, multi-centre, 2-cohort study assessing both minimal residual disease (MRD)-guided discontinuation and fixed duration therapy with IMBRUVICA® in combination with venetoclax, conducted in adult patients who were 70 years or younger with previously untreated active CLL.[1] The study enrolled 323 patients; of these, 159 patients were enrolled to fixed duration therapy consisting of 3 cycles of single agent IMBRUVICA® followed by IMBRUVICA® in combination with venetoclax for 12 cycles.[1] The primary endpoint in the fixed duration cohort was complete response (CR) rate as assessed by the investigator.[1]

About Chronic Lymphocytic Leukemia
Chronic lymphocytic leukemia is typically a slow-growing blood cancer that starts in blood stem cells.[2] In 95% of cases of CLL, the abnormal lymphoid stem cells develop into cancerous, or malignant, B lymphocytes.[2] CLL is more common in men and occurs mainly in people over 60 years of age.[3]

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.

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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 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 1, 2023, 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.

** Dr. Chen was not compensated for any media work. She has been compensated as a consultant.

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