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Health Canada Authorizes TECVAYLI™ (teclistamab injection), a First-in-Class Bispecific Antibody for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma

Approval for TECVAYLI™, a subcutaneously administered therapy, is based on results from the Phase 1/2 MajesTEC-1 study that showed deep and durable responses in triple-class exposed patients with relapsed or refractory multiple myeloma.[1]

Toronto, August 2, 2023/CNW/ - The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that Health Canada has issued a Notice of Compliance with conditions (NOC/c) for TECVAYLI™ (teclistamab injection) for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.[2] TECVAYLI™ has been issued market authorization with conditions, pending the results of trials to verify its clinical benefit.[2] Teclistamab is a bispecific antibody that targets the CD3 receptor expressed on the surface of T-cells and B-cell maturation antigen (BCMA) expressed on the surface of malignant multiple myeloma cells. With its dual binding sites, teclistamab is able to draw CD3+ T-cells in close proximity to BCMA+ cells, resulting in T-cell activation and subsequent lysis and death of BCMA+ cells, which is mediated by secreted perforin and various granzymes stored in the secretory vesicles of cytotoxic T-cells.[2]

Multiple myeloma is the second most common form of blood cancer in Canada with an estimated 1,650 deaths in 2022.[3,4] Every day, 11 Canadians are diagnosed with myeloma.[5]

The introduction of novel therapies in recent years has led to the significant improvement of progression-free survival (PFS) and overall survival (OS) in patients with multiple myeloma.[6] However, the disease remains an incurable blood cancer, with nearly all patients relapsing and requiring subsequent therapy.[6] As the disease progresses, patients experience cycles of relapse and remission, with periods of remission becoming progressively shorter with each new line of therapy.[7,8]

"This Health Canada approval is significant in providing a new treatment option that results in deep and durable responses in patients with this hard-to-treat disease." says Dr. Nizar Bahlis*, Associate Professor, Hematology and Oncology, University of Calgary. "Teclistamab has been shown to result in clinically significant and long-lasting responses. It has the potential to provide substantial clinical benefit to patients with multiple myeloma who have received three prior lines of therapy."

"The approval of TECVAYLI™ is a significant milestone for Canadians living with multiple myeloma," says Martine Elias**, Executive Director, Myeloma Canada. "This new innovative immunotherapy offers hope for a better life for patients whose disease has progressed and are running out of available options after having received three prior lines of treatments."

The Health Canada NOC/c is based on results from the single-arm, open-label, multicenter, Phase 1/2 MajesTEC-1 study, evaluating the safety and efficacy of teclistamab in adults with relapsed or refractory multiple myeloma.[2] Among 125 patients who received the pivotal dose of teclistamab in Phase 2, 76.8 per cent had triple-class refractory disease (median, five previous therapy lines).[2] Patients received a weekly subcutaneous injection of teclistamab at a dose of 1.5 mg/kg, after receiving step-up doses of 0.06 mg/kg and 0.3 mg/kg.[2] The primary endpoint was the overall response rate (partial response or better) as assessed by an independent review committee.[2] Key secondary endpoints included the duration of response; a very good partial response or better; a complete response or better; a stringent complete response; the time to response; PFS and OS; and safety, pharmacokinetic parameters, and immunogenicity.[1]

With a median follow-up of 14.1 months (n=125), the overall response rate (ORR) was 62.4 per cent (95 percent confidence interval [CI]; range, 53.3 –70.9).[2] Notably, 57.6 per cent achieved a very good partial response (VGPR) or better and 36.8 percent achieved a complete response (CR) or better.[2] The median time to the first confirmed response was 1.2

months (range, 0.2–5.5).[2] Responses were deep and durable in patient population, with the median duration of response of 14.9 months (95 percent CI; range, 14.9–not estimable for responders).[2]

The most common AEs were pyrexia (79 per cent), hypogammaglobulinemia (75 per cent), cytokine release syndrome (CRS) (72 per cent), neutropenia (71 per cent), anemia (55 per cent), musculoskeletal pain (52 per cent), fatigue (41 per cent) and thrombocytopenia (40 per cent).[2] Most CRS events were Grade 1 (50 per cent) and Grade 2 (21 per cent). Less than one percent of CRS events were Grade 3, and no Grade 4 or fatal events occurred.[2] Serious adverse reactions were reported in 65 per cent of patients who received TECVAYLI™.[2] Neurologic toxicities were mostly low grade and were reported in 15 per cent of patients. Immune effector cell-associated neurotoxicity syndrome was reported in 3 per cent of patients.[2]

"Today's milestone further strengthens our resolve to discover and develop best-in-class therapies, particularly for incurable forms of cancer where patients face poor outcomes and have limited treatment options," says Berkeley Vincent, President, Janssen Inc. "TECVAYLI™ is an important addition to our growing multiple myeloma portfolio and underscores our commitment to provide combination regimens and treatment sequencing strategies at each line of therapy to optimize patient outcomes over the course of the disease."

From the first approval for VELCADE® (bortezomib for injection) in 2005[9] followed by DARZALEX® (daratumumab for injection) in 2016[10], DARZALEX® SC (daratumumab injection) in 2020[11] and CARVYKTI™ (ciltacabtagene autoleucel) in 2023[12], Janssen has continued to advance and apply the most compelling science, leading to Janssen's fifth approved treatment for multiple myeloma with TECVAYLI™. This signifies the company's significant contribution and deep commitment to developing novel treatment approaches for this fatal form of blood cancer.

About TECVAYLI™

TECVAYLI™ (teclistamab injection) is a bispecific antibody.[2] Teclistamab, a subcutaneous injection, targets both CD3 expressed on the surface of T-cells and BCMA expressed on the surface of myeloma cells, thus mediating T-cell activation and subsequent lysis of BCMA-expressing myeloma cells.[2] TECVAYLI™ (teclistamab injection) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on

the last therapy.[2] TECVAYLI™ (teclistamab injection) has been issued market authorization with conditions, pending the results of trials to verify its clinical benefit.[2]

Products authorized under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. These products have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, these products either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.[2]

Teclistamab is currently being evaluated in several monotherapy and combination studies.[13,14,15,16]

About the MajesTEC-1 Study

MajesTEC-1 is a Phase 1/2 single-arm, open-label, multicohort, multicenter dose-escalation study to evaluate the safety and efficacy of TECVAYLI™ in adults with relapsed or refractory multiple myeloma who received three prior lines of therapy.[2]

Phase 1 of the study (NCT03145181) was conducted in two parts: dose escalation (Part 1) and dose expansion (Part 2).[17] It evaluated safety, tolerability and preliminary efficacy of TECVAYLI™ in adult participants with relapsed or refractory multiple myeloma.[17] To be eligible patients must have previously received at least three lines of therapy (including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody) and have had progressive, measurable disease at screening.[17] Previous treatment with a BCMA-targeted therapy was not allowed.[17] Eligible patients had a score of 0 or 1 on the Eastern Cooperative Oncology Group performance-status scale.[17]

Phase 2 of the study (NCT04557098) evaluated the efficacy of TECVAYLI™ at the recommended phase 2 dose (RP2D), established at subcutaneous 1.5 mg/kg weekly, as measured by ORR.[2,18] Patients received weekly treatment with the recommend dose of TECVAYLI™ (1.5 mg/kg) administered subcutaneously once weekly, preceded by step-up doses of 0.06 mg/kg and 0.3 mg/kg. Patients were treated until disease progression or unacceptable toxicity.[2]

The primary endpoint was overall response rate, which was defined as a partial response or better according to the criteria of the International Myeloma Working Group, as assessed by an independent review committee.[2] Secondary endpoints included duration of response,

very good partial response or better rate, complete response or better rate, stringent complete response rate, time to response, PFS, OS, safety, pharmacokinetic parameters and immunogenicity.[1]

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 TECVAYLI™ (teclistamab injection). 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 http://www.sec.gov/, http://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. Nizar Bahlis was not compensated for this media work. He has been compensated previously by Janssen for other professional engagements.

**Martine Elias was not compensated for this media work. She has been compensated previously by Janssen for other professional engagements.

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