GILEAD RECEIVES APPROVAL IN CANADA FOR YESCARTA™ (AXICABTAGENE CILOLEUCEL) CAR T THERAPY FOR ADULTS WITH RELAPSED OR REFRACTORY LARGE B-CELL LYMPHOMA AFTER TWO OR MORE LINES OF SYSTEMIC THERAPY

– YESCARTA is a chimeric antigen receptor T (CAR T) cell therapy that is custom-made for each patient from his or her own T cells –

– Once reinfused into the patient, the CAR T cells are able to find and attack cancer cells that normal T cells cannot detect –

MISSISSAUGA, ON, Feb. 19, 2019 – Gilead Sciences Canada, Inc. announced today that Health Canada has granted a Notice of Compliance (NOC) for Yescarta™ (axicabtagene ciloleucel), a new chimeric antigen receptor T (CAR T) cell therapy for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (transformed follicular lymphoma, or TFL).[1] YESCARTA is not indicated for the treatment of patients with primary central nervous system lymphoma.

YESCARTA is a CAR T cell therapy, also known as a form of immunotherapy, that is custom-made for each patient from his or her own T cells – a type of white blood cell that is part of the immune system and that recognizes and kills foreign cells. The process works by removing the patient's T cells and genetically altering them with chimeric antigen receptors (CARs). Once reinfused into the patient, the CAR T cells are able to find and attack cancer cells that normal T cells cannot detect.

This cell therapy induces complete response (no detectable cancer) in a proportion of patients with relapsed or refractory DLBCL and primary mediastinal large B-cell lymphoma, which are aggressive forms of non-Hodgkin lymphoma (NHL).

"CAR T therapy is at the forefront of personalized medicine and in the treatment of lymphoid cancers," said Dr. John Kuruvilla, MD, FRCPC, ZUMA-1 Investigator and Hematologist in the Division of Medical Oncology and Hematology at Princess Margaret Hospital. "I have seen first-hand how YESCARTA has transformed the prognosis and outlook for a patient who would otherwise have limited treatment options. This treatment offers a reliable process that is completely customized for each individual patient."

NHL is the fifth most common cancer diagnosed in Canada.[2] In 2017, an estimated 8,300 Canadians were diagnosed with NHL and 2,700 Canadians died from the disease.[3] DLBCL is the most common aggressive type of NHL and accounts for about 30-40 per cent of all cases.[4] Historically, when treated with the current standard of care, patients with relapsed or refractory large B-cell lymphoma had a median overall survival of approximately six months, with only seven per cent attaining a complete response.[5] Currently, patients with large B-cell lymphoma in second or later lines of therapy have poor outcomes and high unmet need, since nearly half of them either do not respond or relapse shortly after transplant.

"There is an unmet need for new therapies for patients with relapsed or refractory large B-cell lymphoma and who face an unfavourable prognosis," said Elizabeth Lye, Director of Research & Programs at Lymphoma Canada. "This approval is an important milestone as it provides new hope for Canadians living with this disease."

YESCARTA will be manufactured by Kite, a Gilead Company (Kite) at its commercial manufacturing facility in El Segundo, California. In the ZUMA-1 pivotal trial, Kite demonstrated a 99 per cent manufacturing success rate with a median manufacturing turnaround time of 17 days[6].

"This regulatory approval brings YESCARTA one step closer to adult Canadian patients with relapsed or refractory large B-cell lymphoma who currently have few or no treatment options available to them," said John McHutchison, AO, MD, Chief Scientific Officer, Head of Research and Development, Gilead Sciences. "YESCARTA brings a new and exciting option to patients and the physicians who treat them."

YESCARTA Pivotal Trial Results

The approval of YESCARTA was based on the ZUMA-1 pivotal trial. In the single-arm trial, 72 per cent of patients (n=73/101) who received YESCARTA responded to therapy, with 51 per cent (n=52/101) achieving a complete response (as assessed by an independent review committee, median follow-up of 15.4 months).

In the study, 12 per cent of patients experienced Grade 3 or higher cytokine release syndrome (CRS) and 31 per cent experienced Grade 3 or higher neurologic adverse reactions. The most common Grade 3 or higher adverse reactions include encephalopathy (30%), unspecified pathogen infection (19%), CRS (12%), bacterial infection (8%), aphasia (7%), viral infection (6%), delirium (6%), hypotension (6%) and hypertension (6%). Grade 5 (fatal) adverse events were reported in 4 patients (anoxic brain injury [secondary to cardiac arrest which occurred in the setting of CRS], histiocytosis haematophagic (HLH), intracranial hemorrhage in the setting of thrombocytopenia and pulmonary embolism).

Serious adverse reactions occurred in 55 per cent of patients. The most common serious adverse reactions (≥ 2%) include encephalopathy (18%), lung infection (7%), pyrexia (7%), pneumonia (6%), confusional state (5%), febrile neutropenia (5%), aphasia (4%), atrial fibrillation (4%), cardiac arrest (4%), urinary tract infection (4%), acute kidney injury (3%), agitation (3%), ejection fraction decreased (3%), hypotension (3%), hypoxia (3%), neutropenia (3%), somnolence (3%), atrial flutter (2%) and delirium (2%). Seventeen (16%) patients required intensive care unit admission.

The most common non-hematological adverse reactions (in ≥ 20%) include CRS (93%), encephalopathy (58%), fatigue (43%), decreased appetite (41%), fever (40%), headache (40%), diarrhea (35%), nausea (31%), tremor (31%), tachycardia (29%), cough (29%), unspecified pathogen infection (28%), hypotension (27%), vomiting (23%), dizziness (21%), constipation (20%), and edema (20%).

IMPORTANT SAFETY INFORMATION

The YESCARTA Product Monograph has a SERIOUS WARNINGS AND PRECAUTIONS BOX regarding the risks of CYTOKINE RELEASE SYNDROME and NEUROLOGIC ADVERSE REACTIONS

- **Cytokine Release Syndrome (CRS)**, including fatal or life-threatening reactions, occurred in patients receiving YESCARTA. Delay YESCARTA treatment if a patient has active uncontrolled infection or inflammatory disorders, active graft-versus-host disease (GVHD) or unresolved serious adverse reactions from prior therapies. Monitor for CRS after treatment with YESCARTA. Provide supportive care, tocilizumab, or tocilizumab and corticosteroids, as needed.
- **Neurologic adverse reactions,** including fatal or life-threatening reactions, occurred in patients receiving YESCARTA, including concurrently with CRS or independently of CRS. Monitor for neurologic adverse reactions after treatment with YESCARTA. Provide supportive care, tocilizumab (if with concurrent CRS), or corticosteroids, as needed.
- YESCARTA should be administered by experienced health professionals at specialized treatment centres

Cytokine Release Syndrome (CRS)

CRS, including fatal or life-threatening reactions, occurred following treatment with YESCARTA. In ZUMA-1, CRS occurred in 93% of patients receiving YESCARTA, including ≥ Grade 3 (Lee grading system) CRS in 12% of patients. The median time to onset was 2 days (range: 1 to 12 days) and the median duration of CRS was 7 days (range: 2 to 29 days, with the exception of one observation of 58 days). The most common manifestations of CRS (>10%) include fever (76%), hypotension (41%), tachycardia (21%), hypoxia (21%), and chills (19%). CRS can cause end organ dysfunctions. Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation/flutter and ventricular tachycardia), hypoxia, hypotension, ejection fraction decreased, cardiac arrest, cardiac failure, renal insufficiency/failure, metabolic acidosis, aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, coagulopathy, capillary leak syndrome, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS).

Ensure that 4 doses of tocilizumab are available prior to infusion of YESCARTA. Monitor patients at least daily for 7 days at the specialized healthcare facility following infusion for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for 4 weeks after infusion. Counsel patients to remain within proximity of a specialized clinical facility for at least 4 weeks and seek immediate medical attention should signs or symptoms of CRS occur at any time. At the first sign of CRS, institute treatment with supportive care, tocilizumab or tocilizumab and corticosteroids as indicated.

Neurologic

Severe neurologic adverse reactions have been very commonly observed in patients treated with YESCARTA, which could be life-threatening or fatal. Neurologic adverse reactions occurred in 65% of patients, 31% of whom experienced Grade 3 or higher (severe or life threatening) adverse reactions. The median time to onset was 5 days (range 1 to 17 days). The median duration was 13 days, with a range of 1 to 191 days. Ninety-eight per cent (98%) of all patients recovered from neurologic adverse reactions.

The most common signs or symptoms (>10%) associated with neurologic adverse reactions include encephalopathy (37%), tremor (31%), confusional state (27%), aphasia (18%), and somnolence (17%). Serious adverse reactions including encephalopathy, aphasia, delirium, and seizures have been reported in patients administered YESCARTA. Fatal and serious cases of cerebral edema have been reported in patients treated with YESCARTA.

Patients with a history of CNS disorders such as seizures or cerebrovascular ischemia may be at increased risk.

Hypersensitivity Reactions

Allergic reactions may occur with the infusion of YESCARTA. Serious hypersensitivity reactions including anaphylaxis, may be due to dimethyl sulfoxide (DMSO) or residual gentamicin in YESCARTA.

Serious Infections

Severe or life-threatening infections occurred in patients after YESCARTA infusion. In ZUMA-1, infections (all grades) occurred in 38% of patients. Grade 3 or higher infections occurred in 25% of patients, including infections with an unspecified pathogen, bacterial infections, and viral infections. YESCARTA should not be administered to patients with clinically significant active infections. Monitor patients for signs and symptoms of infection before and after YESCARTA infusion and treat appropriately. Administer prophylactic anti-microbials according to local guidelines.

Febrile neutropenia was observed in 35% of patients after YESCARTA infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids and other supportive care as medically indicated.

Viral Reactivation

Reactivation of hepatitis B virus (HBV) and human herpesvirus 6 (HHV-6) can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing.

Prolonged cytopenias

Patients may exhibit cytopenias for several weeks following lymphodepleting chemotherapy and YESCARTA infusion. In ZUMA-1, Grade 3 or higher prolonged cytopenias (cytopenias not resolved by Day 30 following YESCARTA infusion) included thrombocytopenia (27%), neutropenia (31%), lymphopenia (99%), and anemia (17%). Monitor blood counts after YESCARTA infusion.

Hypogammaglobulinemia

B-cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with YESCARTA. In ZUMA-1, hypogammaglobulinemia occurred in 17% of patients. B-cell aplasia was observed in 60% and 77% of patients at baseline and at 3 months, respectively. Monitor immunoglobulin levels after treatment with YESCARTA and manage using infection precautions, antibiotic prophylaxis and immunoglobulin replacement in case of recurrent infections.

Due to prolonged hypogammaglobulinemia and B-cell aplasia, it is not known if patients will respond to vaccination following treatment with YESCARTA. The safety of immunization with live viral vaccines during or following YESCARTA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during YESCARTA treatment, and until immune recovery following treatment with YESCARTA.

Secondary Malignancies

Patients treated with YESCARTA may develop secondary malignancies. They should be monitored life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact the company to obtain instructions on patient samples to collect for testing.

Driving and Operating Machinery

Due to the potential for neurologic events, including altered mental status or seizures, patients receiving YESCARTA are at risk for altered or decreased consciousness or coordination in the 8 weeks following YESCARTA infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

Endocrine and Metabolism

Tumour lysis syndrome (TLS)

TLS may occur in patients treated with YESCARTA. To minimize the risk of TLS, patients with elevated uric acid or high tumour burden should receive prophylactic treatment (allopurinol, or an alternative prophylaxis) prior to YESCARTA infusion.

Adverse Reactions

For adverse reactions please refer to **YESCARTA Pivotal Trial Results** earlier in this release.

About Kite

Kite, a Gilead Company, is a biopharmaceutical company based in Santa Monica, California. Kite is engaged in the development of innovative cancer immunotherapies. The company is focused on chimeric antigen receptor and T cell receptor engineered cell therapies. For more information on Kite, please visit www.kitepharma.com.

About Gilead Sciences

Gilead Sciences, Inc. is a research-based biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet medical need. The company strives to transform and simplify care for people with life-threatening illnesses around the world. Gilead has operations in more than 35 countries worldwide, with headquarters in Foster City, California. Gilead Sciences Canada, Inc. is the Canadian affiliate of Gilead Sciences, Inc., and was established in Mississauga, Ontario in 2006. For more information on Gilead Sciences, please visit the company's website at www.gilead.com.

Forward-Looking Statement

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the risk that physicians may not see the benefits of prescribing YESCARTA for the approved indications; the ability of Kite to continue to manufacture YESCARTA at the success rates experienced during clinical trials; the availability of certified centers in Canada to provide YESCARTA to patients; and the possibility of unfavorable results from additional clinical trials involving YESCARTA. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended October 31, 2018, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead and Kite, and Gilead and Kite assume no obligation to update any such forward-looking statements.

Canadian Product Monograph for YESCARTA, including Serious Warnings and Precautions Box, is available at www.gilead.ca.

For more information on Gilead Sciences, please visit the company's website at www.gilead.com, follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

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