U.S. FDA Approves Kite’s Tecartus™, the First and Only CAR T Treatment for Relapsed or Refractory Mantle Cell Lymphoma

July 24, 2020

-- 87 Percent of Patients in ZUMA-2 Pivotal Trial Responded to Single Infusion of Tecartus --

-- Kite Becomes First Company with Multiple Approved CAR T Therapies --

SANTA MONICA, Calif.--(BUSINESS WIRE)--Jul. 24, 2020-- Kite, a Gilead Company (Nasdaq: GILD), today announced that the U.S. Food and Drug Administration (FDA) has granted accelerated approval to Tecartus™ (brexucabtagene autoleucel, formerly KTE-X19), the first and only approved chimeric antigen receptor (CAR) T cell therapy for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL). The approval of this one-time therapy follows a priority review and FDA Breakthrough Therapy Designation and is based on results of ZUMA-2, a single-arm, open-label study in which 87 percent of patients responded to a single infusion of Tecartus, including 62 percent of patients achieving a complete response (CR). Among patients evaluable for safety, 18 percent experienced Grade 3 or higher cytokine release syndrome (CRS) and 37 percent experienced Grade 3 or higher neurologic toxicities.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20200724005428/en/

“Despite promising advances, there are still major gaps in treatment for patients with MCL who progress following initial therapy,” said Michael Wang, MD, ZUMA-2 Lead Investigator and Professor, Department of Lymphoma and Myeloma, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center. “Many patients have high-risk disease and are more likely to keep progressing, even after subsequent treatments. The availability of Tecartus as the first-ever cell therapy for patients with relapsed/refractory MCL provides an important option with a response rate of nearly 90 percent and early clinical evidence suggesting durable remissions in later lines of therapy.”

“Kite is committed to bringing the promise of CAR T therapy to patients with hematological cancers, and as such, we are proud to launch our second cell therapy,” said Christi Shaw, Chief Executive Officer of Kite. “I extend my thanks to the patient study participants, caregivers, clinical researchers, regulators and dedicated colleagues at Kite who helped make this approval possible, and we look forward to partnering with the lymphoma community to deliver this potentially transformative therapy to patients with relapsed or refractory MCL.”

Tecartus has a Boxed Warning in its product label regarding the risks of CRS and neurologic toxicities. A Risk Evaluation and Mitigation Strategy (REMS) has been approved by the FDA for Tecartus and has been combined with the Yescarta® (axicabtagene ciloleucel) REMS. The REMS program will inform and educate healthcare professionals about the risks associated with Tecartus therapy, and training and certification on the REMS program will be an integral part of the final authorization for centers offering Tecartus. Additional information about the REMS program can be found at www.YescartaTecartusREMS.com. Please see below for Important Safety Information.

MCL is a rare form of non-Hodgkin lymphoma (NHL) that arises from cells originating in the “mantle zone” of the lymph node and predominantly affects men over the age of 60. MCL is highly aggressive following relapse, with many patients progressing following therapy.

“This approval marks the first CAR T cell therapy approved for mantle cell lymphoma patients and represents a new frontier in the treatment of this disease,” said Meghan Gutierrez, Chief Executive Officer at the Lymphoma Research Foundation. “In the past decade, researchers have made significant progress in our understanding of this disease and we have seen an increase in clinical trials for patients, which we hope will continue to improve treatment strategies and the options available to people with mantle cell lymphoma. Today’s news builds upon this progress and provides hope to mantle cell patients and their loved ones.”

Tecartus will be manufactured in Kite’s commercial manufacturing facility in El Segundo, California. In the ZUMA-2 trial, Kite demonstrated a 96 percent manufacturing success rate and a median manufacturing turnaround time of 15 days from leukapheresis to product delivery. Manufacturing speed is especially critical for patients with advanced disease, who are very ill and at risk for quick progression.

Patients whose healthcare professionals have prescribed Tecartus therapy can work with Kite Konnect®, an integrated technology platform that provides information and assistance throughout the therapy process for Kite’s commercialized CAR T therapies, including courier tracking for shipments and manufacturing status updates. Kite Konnect provides support for eligible patients receiving Yescarta and Tecartus, and it provides information for the healthcare teams supporting their patients. Healthcare providers and patients can reach Kite Konnect at www.KiteKonnect.com or 1-844-454-KITE (1-844-454-5483).

KTE-X19 is currently under review in the European Union and has been granted Priority Medicines (PRIME) designation by the European Medicines Agency for relapsed or refractory MCL.

**Tecartus Trial Results**

The approval of Tecartus is supported by data from the ongoing, single arm, open-label ZUMA-2 pivotal trial. The study enrolled 74 adult patients with relapsed or refractory MCL who had previously received anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody therapy and a Bruton tyrosine kinase inhibitor (ibrutinib or acalabrutinib). The primary endpoint was objective response rate (ORR) per the Lugano Classification (2014), defined as the combined rate of CR and partial responses as assessed by an Independent Radiologic Review Committee (IRRC).

In the study, 87 percent of patients (n=60 evaluable for efficacy analysis) responded to a single infusion of Tecartus, including 62 percent of patients who achieved a CR. Among all patients, follow-up was at least six months after their first objective disease response. Median duration of response has not yet been reached.

In the trial, 18 percent of patients (n=82 evaluable for safety) experienced Grade 3 or higher CRS and 37 percent experienced neurologic events. The most common (≥ 10 percent) Grade 3 or higher adverse reactions were anemia, neutropenia, thrombocytopenia, hypotension, hypophosphatemia,
en cephalopathy, leukopenia, hypoxia, pyrexia, hyponatremia, hypertension, infection-pathogen unspecified, pneumonia, hypocalcemia and lymphopenia. The FDA approved Tecartus with a Risk Evaluation and Mitigation Strategy (REMS). The Tecartus REMS has been combined with the Yescarta REMS and is now called the “Yescarta (axicabtagene ciloleucel) and Tecartus (brexucabtagene autoleucel) REMS Program” (www.YescartaTecartusREMS.com).

About Tecartus

Tecartus is an autologous, anti-CD19 CAR T cell therapy. Tecartus uses the XLP™ manufacturing process that includes T cell enrichment, a necessary step in certain B-cell malignancies in which circulating lymphoblasts are a common feature. In addition to MCL, Tecartus is also currently in Phase 1/2 trials in acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL). The use of Tecartus in ALL and CLL is investigational, and its safety and efficacy have not been established in these cancer types.

Tecartus Indication

Tecartus is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

This indication is approved under accelerated approval based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITIES

- Cytokine Release Syndrome (CRS), including life-threatening reactions, occurred in patients receiving Tecartus. Do not administer Tecartus to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
- Neurologic toxicities, including life-threatening reactions, occurred in patients receiving Tecartus, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with Tecartus. Provide supportive care and/or corticosteroids as needed.
- Tecartus is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Yescarta and Tecartus REMS Program.

Cytokine Release Syndrome (CRS), including life-threatening reactions, occurred following treatment with Tecartus. In ZUMA-2, CRS occurred in 91% (75/82) of patients receiving Tecartus, including ≥ Grade 3 CRS in 18% of patients. Among the patients who died after receiving Tecartus, one had a fatal CRS event. The median time to onset of CRS was three days (range: 1 to 13 days) and the median duration of CRS was ten days (range: 1 to 50 days). Among patients with CRS, key manifestations (>10%) included fever (99%), hypotension (60%), hypoxia (37%), chills (33%), tachycardia (37%), headache (24%), fatigue (19%), nausea (13%), alanine aminotransferase increased (13%), aspartate aminotransferase increased (12%), and diarrhea (11%). Serious events associated with CRS included hypotension, fever, hypoxia, acute kidney injury, and tachycardia.

Ensure that a minimum of two doses of tocilizumab are available for each patient prior to infusion of Tecartus. Following infusion, monitor patients for signs and symptoms of CRS daily for at least seven days at the certified healthcare facility, and for four weeks thereafter. Counsel patients to 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 Toxicities, including those that were life-threatening, occurred following treatment with Tecartus. In ZUMA-2, neurologic events occurred in 81% of patients, 37% of whom experienced Grade ≥3 adverse reactions. The median time to onset for neurologic events was six days (range: 1 to 32 days). Neurologic events resolved for 52 out of 66 (79%) patients with a median duration of 21 days (range: 2 to 454 days). Three patients had ongoing neurologic events at the time of death, including one patient with serious encephalopathy. The remaining unresolved neurologic events were either Grade 1 or Grade 2. Fifty-four (6%) patients experienced CRS by the onset of neurologic events. Five (6%) patients did not experience CRS with neurologic events and eight patients (10%) developed neurological events after the resolution of CRS. 85% of all treated patients experienced the first CRS or neurological event within the first seven days after Tecartus infusion.

The most common neurologic events (>10%) included encephalopathy (51%), headache (35%), tremor (38%), aphasia (23%), and delirium (16%). Serious events including encephalopathy, aphasia, and seizures occurred.

Monitor patients daily for at least seven days at the certified healthcare facility and for four weeks following infusion for signs and symptoms of neurologic toxicities and treat promptly.

REMS Program: Because of the risk of CRS and neurologic toxicities, Tecartus is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Yescarta and Tecartus REMS Program which requires that:

- Healthcare facilities that dispense and administer Tecartus must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of two doses of tocilizumab are available for each patient for infusion within two hours after Tecartus infusion, if needed for treatment of CRS.
- Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer Tecartus are trained in the management of CRS and neurologic toxicities. Further information is available at www.YescartaTecartusREMS.com or 1-844-454-KITE (5483).

Hypersensitivity Reactions: Serious hypersensitivity reactions, including anaphylaxis, may occur due to dimethyl sulfoxide (DMSO) or residual gentamicin in Tecartus.
Severe Infections: Severe or life-threatening infections occurred in patients after Tecartus infusion. In ZUMA-2, infections (all grades) occurred in 56% of patients. Grade 3 or higher infections, including bacterial, viral, and fungal infections, occurred in 30% of patients. Tecartus should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after infusion and treat appropriately. Administer prophylactic antimicrobials according to local guidelines.

Febrile neutropenia was observed in 8% of patients after Tecartus 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
Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, 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 Tecartus infusion. In ZUMA-2, Grade ≥ 3 cytopenias not resolved by Day 30 following Tecartus infusion occurred in 55% of patients and included thrombocytopenia (38%), neutropenia (37%), and anemia (17%). Monitor blood counts after infusion.

Hypogammaglobulinemia and B-cell aplasia can occur in patients receiving treatment with Tecartus. In ZUMA-2, hypogammaglobulinemia occurred in 16% of patients. Monitor immunoglobulin levels after treatment with Tecartus and manage using infection precautions, antibiotic prophylaxis, and immunoglobulin replacement. The safety of immunization with live viral vaccines during or following Tecartus treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least six weeks prior to the start of lymphodepleting chemotherapy, during treatment, and until immune recovery following treatment with Tecartus.

Secondary Malignancies may develop. Monitor life-long for secondary malignancies. In the event that it occurs, contact Kite at 1-844-454-KITE (5483) to obtain instructions on patient samples to collect for testing.

Effects on Ability to Drive and Use Machines: Due to the potential for neurologic events, including altered mental status or seizures, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks following Tecartus infusion. Advise patients to refrain from driving and engaging in hazardous activities, such as operating heavy or potentially dangerous machinery, during this period.

Adverse Reactions: The most common adverse reactions (incidence ≥ 20%) were pyrexia, CRS, hypotension, encephalopathy, fatigue, tachycardia, arrhythmia, infection – pathogen unspecified, chills, hypoxia, cough, tremor, musculoskeletal pain, headache, nausea, edema, motor dysfunction, constipation, diarrhea, decreased appetite, dyspnea, rash, insomnia, pleural effusion, and aphasia. Serious adverse reactions occurred in 66% of patients. The most common serious adverse reactions (> 2%) were encephalopathy, pyrexia, infection – pathogen unspecified, CRS, hypoxia, aphasia, renal insufficiency, pleural effusion, respiratory failure, bacterial infections, dyspnea, fatigue, arrhythmia, tachycardia, and viral infections.

Please see full Prescribing Information, including BOXED WARNING and Medication Guide.

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. 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 and patients may not see the potential benefits of Tecartus therapy and the possibility of unfavorable results from other ongoing and additional clinical studies involving Tecartus for the treatment of adult patients with relapsed or refractory MCL and other potential indications. There is also the risk that the European Commission may not approve KTE-X19 for the treatment of relapsed or refractory MCL in the anticipated timelines or at all, and the marketing approval, if granted, may have significant limitations on its use. 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 March 31, 2020, 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.


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For more information on Kite, please visit the company’s website at www.kitepharma.com or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000. Follow Kite on social media on Twitter (@KitePharma) and LinkedIn.

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