



U.S. FDA Approves Kite's Tecartus® as the First and Only Car T for Adults With Relapsed or Refractory B-cell Acute Lymphoblastic Leukemia

October 1, 2021

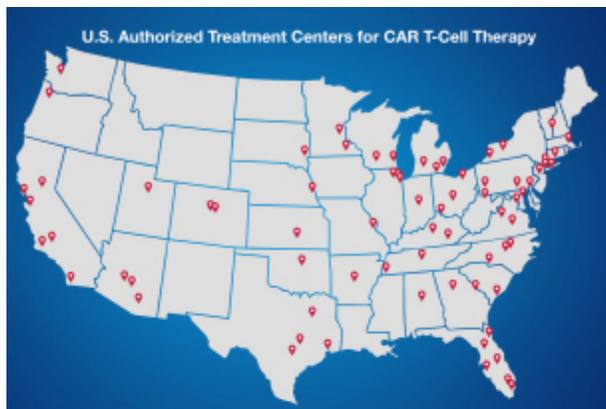
-- 65% of Patients Achieved Overall Complete Remission with Tecartus --

-- High Unmet Need: Fifty Percent of Adult Patients Will Relapse on Currently Available Treatments --

-- Approval Marks Kite's Fourth Indication for its Cell Therapies and First in Leukemia --

SANTA MONICA, Calif.--(BUSINESS WIRE)--Oct. 1, 2021-- Kite, a Gilead Company (Nasdaq: GILD), today announced the U.S. Food and Drug Administration (FDA) has granted approval for Tecartus® (brexucabtagene autoleucel) for the treatment of adult patients (18 years and older) with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). Following FDA Breakthrough Therapy Designation and a priority review, Tecartus is the first and only chimeric antigen receptor (CAR) T-cell therapy approved for adults (18 years and older) with ALL. There is a high unmet need, as half of this patient population will relapse, and median overall survival (OS) is only approximately eight months with current standard-of-care treatments. Patients can [access](#) Tecartus through 109 authorized treatment centers across the U.S.

This press release features multimedia. View the full release here: <https://www.businesswire.com/news/home/20211001005719/en/>



"Adults with ALL face a significantly poorer prognosis compared to children, and roughly half of all adults with B-ALL will relapse on currently available therapies," said Bijal Shah, MD, ZUMA-3 investigator and medical oncologist, Moffitt Cancer Center, Tampa, Florida. "We now have a new meaningful advancement in treatment for these patients. A single infusion of Tecartus has demonstrated durable responses, suggesting the potential for long-term remission and a new approach to care."

The approval is based on results from ZUMA-3, a global, multicenter, single-arm, open-label study in which 65% of the evaluable patients (n=54) achieved complete remission (CR) or CR with incomplete hematological recovery (CRi) at a median actual follow-up of 12.3 months. The duration of CR was estimated to exceed 12 months for more than half the patients. Among efficacy-evaluable patients, median duration of remission (DOR) was 13.6 months. Among the patients treated with Tecartus at the target dose (n=78), Grade 3 or higher cytokine release syndrome (CRS) and neurologic events occurred in 26% and 35% of patients, respectively, and were generally well-managed.

"Today marks Kite's fourth FDA approved indication in cell therapy in under four years, demonstrating our commitment to advancing CAR T for patients across many different hematologic malignancies," said Christi Shaw, Chief Executive Officer of Kite. "Tecartus has already transformed outcomes for adults living with mantle cell lymphoma, and we look forward to offering the hope for a cure to patients with ALL."

Adults with relapsed or refractory ALL often undergo multiple treatments including chemotherapy, targeted therapy and stem cell transplant. CAR T-cell therapy works differently, by harnessing a patient's own immune system to fight cancer. With CAR T, the patient's blood is drawn and the T cells are separated. Then the T cells are genetically engineered with a specific receptor that enables them to identify and attack cancer cells, and put back into the patient's body.

"Roughly half of all ALL cases actually occur in adults, and unlike pediatric ALL, adult ALL has historically had a poor prognosis," said Lee Greenberger, PhD, Chief Scientific Officer of The Leukemia & Lymphoma Society (LLS). "Developing new therapies that would be life-changing for people with cancer has been a dream of LLS. We are proud to see the potential of CAR T realized for even more people with this approval for brexucabtagene autoleucel."

Tecartus is also currently under review in the European Union and United Kingdom for the treatment of adult patients with relapsed or refractory B-cell precursor ALL.

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Kite
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US Authorized Treatment Centers for CAR T-Cell Therapy
(Graphic: Kite)

The Tecartus U.S. Prescribing Information has a BOXED WARNING for the risks of CRS and neurologic toxicities, and Tecartus is approved with a Risk Evaluation and Mitigation Strategy (REMS) due to these risks; see below for Important Safety Information.

Additional Information About ZUMA-3 Trial

Further efficacy results from the ZUMA-3 trial have been published and presented in scientific forums. Published Phase 1 data showed 32% of responders (n=22) were still in remission at the median follow-up of 22.1 months. In Phase 2 data presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, investigators reported that among treated patients (n=54), 31% of these patients were in ongoing response at a

median follow-up of 16.4 months. 97% of responders had deep molecular remission, with undetectable minimal residual disease (MRD), and median OS among all responders has not yet been reached. A safety analysis, reported in the *Lancet*, showed among all patients who experienced a neurologic event, 94% of CRS events and 88% of neurologic events were resolved.

ZUMA-3 is an international multicenter, registrational Phase 1/2 study in adult patients (≥18 years old) with ALL whose disease is refractory to or has relapsed following first standard systemic therapy with remission of 12 months or less, after two or more lines of systemic therapy or at least 100 days after allogeneic stem cell transplantation. Seventy-one patients were enrolled (and leukapheresed) in the study, and the primary endpoint was overall complete remission rate (OCR, equaling complete remission plus complete remission with incomplete hematologic recovery) as determined by an independent review.

About ALL

ALL is an aggressive type of blood cancer that can also involve the lymph nodes, spleen, liver, central nervous system and other organs. Approximately 1,000 adults are treated annually for relapsed or refractory ALL. B-cell precursor ALL is the most common form, accounting for approximately 75% of cases, and treatment is typically associated with inferior outcomes compared with other types of ALL. Survival rates remain very poor in adult patients with relapsed or refractory ALL, with median OS at less than eight months.

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. Tecartus is also being evaluated in pediatric ALL, where its use is investigational, and its safety and efficacy have not been established.

About Kite

Kite, a Gilead Company, is a global biopharmaceutical company based in Santa Monica, California, with commercial manufacturing operations in North America and Europe. Kite's singular focus is cell therapy to treat and potentially cure cancer. As the cell therapy leader, Kite has more approved CAR T indications to help more patients than any other company. For more information on Kite, please visit www.kitepharma.com.

About Gilead Sciences

Gilead Sciences, Inc. is a biopharmaceutical company that has pursued and achieved breakthroughs in medicine for more than three decades, with the goal of creating a healthier world for all people. The company is committed to advancing innovative medicines to prevent and treat life-threatening diseases, including HIV, viral hepatitis and cancer. Gilead operates in more than 35 countries worldwide, with headquarters in Foster City, California.

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.

- Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

U.S. 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, the key manifestations (>10%) were similar in MCL and ALL and included fever (93%), hypotension (62%), tachycardia (59%), chills (32%), hypoxia (31%), headache (21%), fatigue (20%), and nausea (13%). Serious events associated with CRS included hypotension, fever, hypoxia, tachycardia, and dyspnea.

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 Events, including those that were fatal or life-threatening, occurred following treatment with Tecartus. Neurologic events occurred in 81% (66/82) of patients with MCL, including ≥ Grade 3 in 37% of patients. The median time to onset for neurologic events was six days (range: 1 to 32

days) with a median duration of 21 days (range: 2 to 454 days) in patients with MCL. Neurologic events occurred in 87% (68/78) of patients with ALL, including \geq Grade 3 in 35% of patients. The median time to onset for neurologic events was seven days (range: 1 to 51 days) with a median duration of 15 days (range: 1 to 397 days) in patients with ALL. For patients with MCL, 54 (66%) patients experienced CRS before the onset of neurological events. Five (6%) patients did not experience CRS with neurologic events and eight patients (10%) developed neurological events after the resolution of CRS. Neurologic events resolved for 119 out of 134 (89%) patients treated with Tecartus. Nine patients (three patients with MCL and six patients with ALL) had ongoing neurologic events at the time of death. For patients with ALL, neurologic events occurred before, during, and after CRS in 4 (5%), 57 (73%), and 8 (10%) of patients; respectively. Three patients (4%) had neurologic events without CRS. The onset of neurologic events can be concurrent with CRS, following resolution of CRS or in the absence of CRS.

The most common neurologic events ($>10\%$) were similar in MCL and ALL and included encephalopathy (57%), headache (37%), tremor (34%), confusional state (26%), aphasia (23%), delirium (17%), dizziness (15%), anxiety (14%), and agitation (12%). Serious events including encephalopathy, aphasia, confusional state, and seizures occurred after treatment with Tecartus.

Monitor patients daily for at least seven days for patients with MCL and at least 14 days for patients with ALL 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. Infections (all grades) occurred in 56% (46/82) of patients with MCL and 44% (34/78) of patients with ALL. Grade 3 or higher infections, including bacterial, viral, and fungal infections, occurred in 30% of patients with ALL and MCL. Tecartus should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after Tecartus infusion and treat appropriately. Administer prophylactic antimicrobials according to local guidelines.

Febrile neutropenia was observed in 6% of patients with MCL and 35% of patients with ALL after Tecartus infusion and may be concurrent with CRS. The febrile neutropenia in 27 (35%) of patients with ALL includes events of "febrile neutropenia" (11 (14%)) plus the concurrent events of "fever" and "neutropenia" (16 (21%)). In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids, and other supportive care as medically indicated.

In immunosuppressed patients, life-threatening and fatal opportunistic infections have been reported. The possibility of rare infectious etiologies (e.g., fungal and viral infections such as HHV-6 and progressive multifocal leukoencephalopathy) should be considered in patients with neurologic events and appropriate diagnostic evaluations should be performed.

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 patients with MCL, Grade 3 or higher cytopenias not resolved by Day 30 following Tecartus infusion occurred in 55% (45/82) of patients and included thrombocytopenia (38%), neutropenia (37%), and anemia (17%). In patients with ALL who were responders to Tecartus treatment, Grade 3 or higher cytopenias not resolved by Day 30 following Tecartus infusion occurred in 20% (7/35) of the patients and included neutropenia (12%) and thrombocytopenia (12%); Grade 3 or higher cytopenias not resolved by Day 60 following Tecartus infusion occurred in 11% (4/35) of the patients and included neutropenia (9%) and thrombocytopenia (6%). Monitor blood counts after Tecartus infusion.

Hypogammaglobulinemia: B cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with Tecartus. Hypogammaglobulinemia was reported in 16% (13/82) of patients with MCL and 9% (7/78) of patients with ALL. 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 Tecartus treatment, and until immune recovery following treatment with Tecartus.

Secondary Malignancies may develop. Monitor life-long for secondary malignancies. In the event that one 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 non-laboratory adverse reactions ($\geq 20\%$) were fever, cytokine release syndrome, hypotension, encephalopathy, tachycardia, nausea, chills, headache, fatigue, febrile neutropenia, diarrhea, musculoskeletal pain, hypoxia, rash, edema, tremor, infection with pathogen unspecified, constipation, decreased appetite, and vomiting. The most common serious adverse reactions ($\geq 2\%$) were cytokine release syndrome, febrile neutropenia, hypotension, encephalopathy, fever, infection with pathogen unspecified, hypoxia, tachycardia,

bacterial infections, respiratory failure, seizure, diarrhea, dyspnea, fungal infections, viral infections, coagulopathy, delirium, fatigue, hemophagocytic lymphohistiocytosis, musculoskeletal pain, edema, and paraparesis.

Please see full [Prescribing Information](#), including **BOXED WARNING** and Medication Guide.

Forward-Looking Statements

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 for the treatment of adult patients with relapsed or refractory B-cell ALL; the possibility of unfavorable results from ongoing and additional clinical trials involving Tecartus; and the possibility that Tecartus may not receive regulatory approvals in the European Union and United Kingdom for the treatment of adult patients with relapsed or refractory B-cell ALL in the anticipated timelines or at all, and the risk that any such approvals, if granted, may have significant limitation on its use. These and other risks, uncertainties and other factors are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, as filed with the U.S. Securities and Exchange Commission. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Investors are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties and are cautioned not to place undue reliance on these forward-looking statements. All forward-looking statements are based on information currently available to Kite and Gilead, and Kite and Gilead assume no obligation and disclaim any intent to update any such forward-looking statements.

*U.S. Prescribing Information for Tecartus including **BOXED WARNING**, is available at www.kitepharma.com and www.gilead.com.*

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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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