New Data for Tecartus™ Demonstrate Durable Responses at One Year Follow-Up in Relapsed or Refractory Mantle Cell Lymphoma

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-- Median Overall Survival Still Not Reached After Single Infusion of Tecartus in Pivotal ZUMA-2 Trial --

-- Significant and Durable Rate of Complete Response Further Supports Tecartus as First and Only CAR T-Cell Therapy in Relapsed or Refractory MCL --

SANTA MONICA, Calif.--(BUSINESS WIRE)--Dec. 5, 2020-- Kite, a Gilead Company (Nasdaq: GILD), today announced follow-up results from the pivotal ZUMA-2 trial of Tecartus™ (brexucabtagene autoleucel, formerly KTE-X19) in adult patients with relapsed or refractory mantle cell lymphoma (MCL). At a median follow-up of 17.5 months (n=60 evaluable for efficacy), 92 percent of patients had achieved a response, including 67 percent with a complete response (CR). Secondary endpoints of median duration of response, progression-free survival (PFS) and overall survival (OS) all were not yet reached. These data were presented at the 62nd ASH Annual Meeting and Exposition (Abstract #1120).

“Patients with mantle cell lymphoma face a disease that often becomes more aggressive over time and nearly always relapses after initial therapy,” said Michael Wang, MD, Puddin Clarke Endowed Professor, Department of Lymphoma and Myeloma at The University of Texas MD Anderson Cancer Center. “Many patients with relapsed or refractory MCL will have high-risk disease that is more likely to keep progressing after treatment, so our goal with any therapy is to provide durable remission. With more than half of the patients in the ZUMA-2 trial still alive at nearly one and a half years after infusion, these results reinforce brexucabtagene autoleucel's potential to address the gap in existing treatment.”

Among all efficacy-evaluable patients (n=60), 48 percent had ongoing responses at data cut-off. Estimates for PFS and OS at 15 months were 59 percent and 76 percent, respectively. The first 28 patients treated had a median follow-up of 32.3 months, and 39 percent of these patients remain in remission with no further therapy.

Among all patients (n=68), Grade 3 or higher cytokine release syndrome (CRS) and neurologic events (NE) occurred in 15 percent and 31 percent of patients, respectively. No new Grade 5 events occurred with additional follow-up.

“These Tecartus data build on the significant response rates seen previously with an impressive durability, which continues to show that we have a potentially transformative treatment option for patients with relapsed or refractory MCL,” said Ken Takeshita, MD, Kite’s Global Head of Clinical Development. “As we continue to observe longer-term results with Tecartus, as well as with the most recent four-year results for Yescarta, our first CAR T-cell therapy, we are encouraged by the unparalleled long-term survival benefits that may be possible with these cell therapies.”

In July, Tecartus became the first CAR T-cell therapy to receive accelerated approval from the FDA for the treatment of relapsed or refractory mantle cell lymphoma, based on overall response rate and durability of response. Continued approval for this indication may be contingent upon additional data from a confirmatory trial. The Tecartus U.S. Prescribing Information has a Boxed Warning in its product label regarding 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 Indication and Important Safety Information.

About Mantle Cell Lymphoma

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.

About ZUMA-2

ZUMA-2 is an ongoing, single arm, open-label trial that 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 is 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).

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 (66%) patients experienced CRS by the onset of neurological events. Five (8%) 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 6% 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.
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 Yescarta

Yescarta is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including DLBCL not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitation of Use: Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

U.S. Important Safety Information for Yescarta

BOXED WARNING: CYTOKINE RELEASE SYNDROME AND NEUROLOGIC TOXICITIES

- Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving Yescarta. Do not administer Yescarta to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
- Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving Yescarta, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with Yescarta. Provide supportive care and/or corticosteroids as needed.
- Yescarta 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) occurred in 94% of patients, with 13% ≥ Grade 3. Among patients who died after receiving Yescarta, 4 had ongoing CRS at death. The median time to onset was 2 days (range: 1-12 days) and median duration was 7 days (range: 2-50 days). Key manifestations include fever (78%), hypotension (41%), tachycardia (28%), hypoxia (22%), and chills (20%). Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome. Ensure that 2 doses of tocilizumab are available prior to Yescarta infusion. Following infusion, monitor patients for signs and symptoms of CRS at least daily for 7 days at the certified healthcare facility, and for 4 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 occurred in 87% of patients, 98% of which occurred within the first 8 weeks with a median time to onset of 4 days (range: 1-43 days) and a median duration of 17 days. Grade ≥3 occurred in 31% of patients. The most common neurologic toxicities included encephalopathy (57%), headache (44%), tremor (31%), dizziness (21%), aphasia (18%), delirium (17%), insomnia (9%), and anxiety (9%). Prolonged encephalopathy lasting up to 173 days was noted. Serious events including leukoencephalopathy and seizures, as well as fatal and serious cases of cerebral edema have occurred. Following Yescarta infusion, monitor patients for signs and symptoms of neurologic toxicities at least daily for 7 days at the certified healthcare facility, and for 4 weeks thereafter, and treat promptly.

REMS: Because of the risk of CRS and neurologic toxicities, Yescarta is available only through a restricted program called the Yescarta and Tecartus REMS Program which requires that: Healthcare facilities that dispense and administer Yescarta must be enrolled and comply with the REMS requirements and must have on-site, immediate access to a minimum of 2 doses of tocilizumab for each patient for infusion within 2 hours after Yescarta infusion, if needed for treatment of CRS. Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer Yescarta are trained about the management of CRS and neurologic toxicities. Further information is available at www.YescartaTecartusREMS.com or 1-844-454-KITE (5483).

HYPERSENSITIVITY REACTIONS: Allergic reactions, including serious hypersensitivity reactions or anaphylaxis, may occur with the infusion of Yescarta.

SERIOUS INFECTIONS: Severe or life-threatening infections occurred. Infections (all grades) occurred in 38% of patients. Grade ≥3 infections occurred in 23% of patients; those due to an unspecified pathogen occurred in 16% of patients, bacterial infections in 9%, and viral infections in 4%. Yescarta 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 anti-microbials according to local guidelines. Febrile neutropenia was observed in 36% of patients 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. 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 Yescarta infusion. Grade ≥3 cytopenias not resolved by Day 30 following Yescarta infusion occurred in 28% of patients and included thrombocytopenia (18%), neutropenia (15%), and anemia (3%). Monitor blood counts after infusion.
HYPOGAMMAGLOBULINEMIA and B-cell aplasia can occur. Hypogammaglobulinemia occurred in 15% of patients. Monitor immunoglobulin levels after treatment and manage using infection precautions, antibiotic prophylaxis, and immunoglobulin replacement. 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.

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 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.

ADVERSE REACTIONS: The most common (incidence ≥20%) include CRS, fever, hypotension, encephalopathy, tachycardia, fatigue, headache, decreased appetite, chills, diarrhea, febrile neutropenia, infections-pathogen unspecified, nausea, hypoxia, tremor, cough, vomiting, dizziness, constipation, and cardiac arrhythmias.

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 September 30, 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.

U.S. Prescribing Information for Tecartus and Yescarta, including BOXED WARNINGS, 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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