# Kite Announces Long-Term Data From Pivotal ZUMA-1 Study of Yescarta™ (Axicabtagene Ciloleucel) in Patients With Refractory Large B-cell Lymphoma

December 10, 2017

***-- 42 Percent of Patients Remained in Response, Including 40 Percent in Complete Remission, at a Median Follow-up of 15.4 Months --***

***-- Data Presented at the Annual Meeting of the American Society of Hematology and Published in The New England Journal of Medicine --***

ATLANTA--(BUSINESS WIRE)--Dec. 10, 2017-- Kite, a Gilead Company (Nasdaq: GILD), announced long-term follow-up data from the pivotal ZUMA-1 study of Yescarta™ (axicabtagene ciloleucel) in patients with refractory large B-cell lymphoma. With a minimum follow-up of one year after a single infusion of Yescarta (median follow-up of 15.4 months), 42 percent of patients continued to respond to therapy, including 40 percent with a complete remission. Detailed results from this updated analysis were simultaneously presented at the Annual Meeting of the American Society of Hematology (ASH) in Atlanta and published in *The New England Journal of Medicine*.

This press release features multimedia. View the full release here: http://www.businesswire.com/news/home/20171210005072/en/

Yescarta is the first chimeric antigen receptor T (CAR T) cell therapy to be approved by the U.S. Food and Drug Administration (FDA) 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. Yescarta is not indicated for patients with primary central nervous system lymphoma.

DLBCL is the most common aggressive non-Hodgkin lymphoma, accounting for three out of every five cases. In the United States each year, there are approximately 7,500 patients with refractory DLBCL who are eligible for CAR T therapy.

“As observed in the SCHOLAR-1 study, treatment options for patients with refractory large B-cell lymphoma have yielded a median overall survival of just six months, with fewer than ten percent of patients achieving complete remission,” said Sattva S. Neelapu, MD, ZUMA-1 Co-Lead Investigator and Professor, Department of Lymphoma/Myeloma, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center. “The durability of response seen with Yescarta in this long-term follow-up reinforces the major advance that CAR T therapy represents for these patients.”

To evaluate the durability of Yescarta responses, an updated analysis was conducted when patients in ZUMA-1 had been followed for a minimum of one year (n=108). In this updated analysis, 82 percent of patients had responded to Yescarta, including 58 percent of patients who had achieved complete remission. At a median of 15.4 months post-infusion, 42 percent of patients remained in response, including 40 percent in complete remission. The median duration of response was 11.1 months (95 percent CI: 3.9 months to not estimable [NE]); in patients who have achieved a complete remission, the median duration of response was not reached (95 percent CI: NE). Median overall survival had not been reached (95 percent CI: 12 months to NE) with an overall survival rate at 18 months of 52 percent (95 percent CI: 41 to 62).

In the updated analysis, 12 percent of patients experienced Grade 3 or higher cytokine release syndrome (CRS) and 31 percent experienced neurologic toxicities respectively. The most common Grade 3 or higher reactions were neutropenia (79 percent), anemia (45 percent) and thrombocytopenia (40 percent). Ten patients experienced a serious adverse event six months after Yescarta infusion, including eight patients with infections. No new onset CRS or neurologic events related to Yescarta were observed in the updated analysis.

Yescarta has a Boxed Warning in its product label and an associated Risk Evaluation and Mitigation Strategy (REMS) regarding the risks of CRS and neurologic toxicities. Please see below for Important Safety Information.

“Historically, people with refractory large B-cell lymphoma have not been adequately served by available treatment options,” said David Chang, MD, PhD, Worldwide Head of Research and Development and Chief Medical Officer at Kite. “We are encouraged by the durability and depth of response seen in ZUMA-1 more than a year after treatment with Yescarta, which represents an important advance in the treatment of patients with refractory disease.”

Yescarta has been granted Priority Medicines (PRIME) regulatory support for DLBCL in the European Union. A Marketing Authorization Application (MAA) for axicabtagene ciloleucel is currently under review with the European Medicines Agency (EMA) and potential approval is expected in the first half of 2018.

**U.S. Indication for 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 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.

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

**U.S. Important Safety Information for Yescarta**

**BOXEDWARNING: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 REMS.**

**Cytokine Release Syndrome (CRS)**

CRS, including fatal or life-threatening reactions, occurred following treatment with Yescarta. In Study 1, CRS occurred in 94% (101/108) of patients receiving Yescarta, including ≥ Grade 3 (Lee grading system) CRS in 13% (14/108) of patients. Among patients who died after receiving Yescarta, four had ongoing CRS events at the time of death. 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 58 days). Key manifestations of CRS 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 (HLH/MAS).

Ensure that 2 doses of tocilizumab are available prior to infusion of Yescarta. Monitor patients at least daily for 7 days at the certified 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 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**

Neurologic toxicities, that were fatal or life-threatening, occurred following treatment with Yescarta. Neurologic toxicities occurred in 87% of patients. Ninety-eight percent of all neurologic toxicities occurred within the first 8 weeks of Yescarta infusion, with a median time to onset of 4 days (range: 1 to 43 days). The median duration of neurologic toxicities was 17 days. Grade 3 or higher neurologic toxicities 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 occurred with Yescarta. Fatal and serious cases of cerebral edema have occurred in patients treated with Yescarta.

Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of neurologic toxicities. Monitor patients for signs or symptoms of neurologic toxicities for 4 weeks after infusion and treat promptly.

**Yescarta REMS**

Because of the risk of CRS and neurologic toxicities, Yescarta is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Yescarta REMS. The required components of the Yescarta REMS are:

- Healthcare facilities that dispense and administer Yescarta 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 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.YescartaREMS.com or 1-844-454-KITE (5483).

**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 Study 1, infections (all grades) occurred in 38% of patients. Grade 3 or higher infections occurred in 23% of patients. Grade 3 or higher infections with 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 Yescarta infusion and treat appropriately. Administer prophylactic anti-microbials according to local guidelines.

Febrile neutropenia was observed in 36% 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*

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. In Study 1, Grade 3 or higher 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 Yescarta infusion.

**Hypogammaglobulinemia**

B-cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with Yescarta. In Study 1, hypogammaglobulinemia occurred in 15% of patients. Monitor immunoglobulin levels after treatment with Yescarta 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 with Yescarta.

**Secondary Malignancies**

Patients treated with Yescarta may develop secondary malignancies. Monitor life-long for secondary malignancies. In the event that a secondary malignancy 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 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.

**Adverse Reactions**

The most common adverse reactions (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. Serious adverse reactions occurred in 52% of patients. The most common serious adverse reactions (> 2%) include encephalopathy, fever, lung infection, febrile neutropenia, cardiac arrhythmia, cardiac failure, urinary tract infection, renal insufficiency, aphasia, cardiac arrest, *Clostridium difficile* infection, delirium, hypotension, and hypoxia.

The most common (≥ 10%) Grade 3 or higher reactions include febrile neutropenia, fever, CRS, encephalopathy, infections-pathogen unspecified, hypotension, hypoxia and lung infections.

**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 is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

**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 possibility of unfavorable results from further clinical trials involving Yescarta. In addition, regulatory agencies, including the EMA, may not approve Yescarta in the currently anticipated timelines or at all, and any marketing approvals may have significant limitations on its use. 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. Actual results may differ materially from those currently anticipated due to a number of risks and uncertainties. Risks and uncertainties that could cause the actual results to differ from expectations contemplated by forward-looking statements include risks and uncertainties detailed from time to time in Gilead Sciences, Inc.'s Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 as filed with the 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 and disclaim any intent to update any such forward-looking statements.

*US Prescribing Information for Yescarta, including **BOXED WARNING** and Medication Guide, is available at www.yescarta.com.*

*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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