CARVYKTI® Significantly Improved Minimal Residual Disease Negativity Compared to Standard of Care for Patients with Relapsed or Refractory Multiple Myeloma

December 10, 2024

- *89 percent of evaluable patients achieved minimal residual disease (MRD) negativity with CARVYKTI® after three-year follow-up in CARTITUDE-4 study; the majority in less than 2 months*
- *Results add to the overall survival (OS) benefit recently reported making CARVYKTI® the first and only cell therapy to significantly extend OS versus standard therapies in multiple myeloma*
- *Landmark Phase 3 CARTITUDE-4 study data featured as an oral presentation at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition*

SOMERSET, N.J., Dec. 09, 2024 (GLOBE NEWSWIRE) -- Legend Biotech Corporation (NASDAQ: LEGN) (Legend Biotech), a global leader in cell therapy, announced today new results from the Phase 3 CARTITUDE-4 study that show a single infusion of CARVYKTI® (ciltacabtagene autoleucel; cilta-cel) provided significantly higher rates of minimal residual disease (MRD)-negativity in patients with relapsed or lenalidomide-refractory multiple myeloma who have received at least one prior line of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD, compared to standard therapies of pomalidomide, bortezomib, and dexamethasone (PVd) or daratumumab, pomalidomide, and dexamethasone (DPd).[1] MRD negativity is a prognostic marker of prolonged survival outcomes for patients with multiple myeloma.[1] These results reinforce the clinical value of CARVYKTI® as early as second line and support the recent achievement of overall survival (OS) benefit versus standard therapies[1]. The MRD negativity findings were featured as an oral presentation at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition (Abstract #1032) in San Diego, California.[1]

"The MRD data further underscores the benefits of treatment with CARVYKTI," said Yi Lin, M.D., Ph.D., hematologist and oncologist at Mayo Clinic, Rochester, MN. "These new findings support CARVYKTI as a transformative therapeutic option, leading to improved progression-free survival, overall survival, and now minimal residual disease negativity." ‡

The Phase 3 CARTITUDE-4 study evaluated CARVYKTI® in comparison to standard therapies of PVd or DPd for the treatment of adults with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy, including a PI and IMiD, and who were lenalidomide-refractory. In the trial, 208 adults were randomized to receive CARVYKTI®, and 211 to receive standard therapies.

The study assessed patients for MRD negativity at the 10^{-5} threshold (cilta-cel, n=145, standard therapies, n=103). At a median follow-up of almost three years (34 months), evaluable patients treated with CARVYKTI® achieved an MRD-negativity rate of 89% versus 38% for those treated with standard therapies (P<0.0001). High rates of overall MRD-negativity were rapidly achieved with CARVYKTI® with 69% of MRD-evaluable patients by day 56. At data cutoff, sustained MRD-negative ≥CR of at least 12 months was achieved in 52% of MRD-evaluable patients in the CARVYKTI® arm vs. 10% in the standard of care arm (P<0.0001). A post-hoc comparison of the CARTITUDE-4 and CARTITUDE-1 studies (1-3 versus 3+ prior lines of therapy) showed higher rates of MRD negativity, PFS, and OS were achieved when CARVYKTI® was administered earlier in the treatment regimen.

"The latest MRD data showcases the advances of CARVYKTI and further demonstrates why it is a leading treatment for patients with multiple myeloma," said Ying Huang, Ph. D., Chief Executive Officer of Legend Biotech. "As we strive to transform the therapeutic landscape in cancer and beyond, we are proud of the progress made and will continue our efforts to improve the quality of life for those battling incurable diseases."

Data from CARTITUDE-4 supported the U.S. Food and Drug Administration (FDA) and European Commission (EC) approval of CARVYKTI® earlier this year for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least one prior line of therapy, including a PI, and IMiD, and are refractory to lenalidomide.[1] CARVYKTI® is the first and only BCMA-targeted CAR-T cell therapy approved for the treatment of patients with multiple myeloma who have had at least one prior line of therapy. Globally, CARVYKTI® is now commercially available in five countries and has been utilized by over 4,500 patients.

CARVYKTI® IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED and RECURRENT CYTOPENIA, and SECONDARY HEMATOLOGICAL MALIGNANCIES

Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with CARVYKTI ®. Do not administer CARVYKTI ® to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), which may be fatal or life-threatening, occurred following treatment with CARVYKTI ®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with CARVYKTI ®. Provide supportive care and/or corticosteroids as needed.

Parkinsonism and Guillain-Barré syndrome (GBS) and their associated complications resulting in fatal or life-threatening reactions have occurred following treatment with CARVYKTI ®.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with CARVYKTI ®. HLH/MAS can occur with CRS or neurologic toxicities.

Prolonged and/or recurrent cytopenias with bleeding and infection and requirement for stem cell transplantation for hematopoietic recovery occurred following treatment with CARVYKTI ®.

Secondary hematological malignancies, including myelodysplastic syndrome and acute myeloid leukemia, have occurred in patients following treatment with CARVYKTI ®. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T-cell immunotherapies, including CARVYKTI ®.

CARVYKTI ® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI® REMS Program.

WARNINGS AND PRECAUTIONS

INCREASED EARLY MORTALITY – In CARTITUDE-4, a (1:1) randomized controlled trial, there was a numerically higher percentage of early deaths in patients randomized to the CARVYKTI® treatment arm compared to the control arm. Among patients with deaths occurring within the first 10 months from randomization, a greater proportion (29/208; 14%) occurred in the CARVYKTI® arm compared to (25/211; 12%) in the control arm. Of the 29 deaths that occurred in the CARVYKTI® arm within the first 10 months of randomization, 10 deaths occurred prior to CARVYKTI® infusion, and 19 deaths occurred after CARVYKTI® infusion. Of the 10 deaths that occurred prior to CARVYKTI® infusion, all occurred due to disease progression, and none occurred due to adverse events. Of the 19 deaths that occurred after CARVYKTI® infusion, 3 occurred due to disease progression, and 16 occurred due to adverse events. The most common adverse events were due to infection (n=12).

CYTOKINE RELEASE SYNDROME (CRS), including fatal or life-threatening reactions, occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® for RRMM in the CARTITUDE-1 & 4 studies (N=285), CRS occurred in 84% (238/285), including ≥ Grade 3 CRS (ASCT 2019) in 4% (11/285) of patients. Median time to onset of CRS, any grade, was 7 days (range: 1 to 23 days). CRS resolved in 82% with a median duration of 4 days (range: 1 to 97 days). The most common manifestations of CRS in all patients combined (≥ 10%) included fever (84%), hypotension (29%) and aspartate aminotransferase increased (11%). Serious events that may be associated with CRS include pyrexia, hemophagocytic lymphohistiocytosis, respiratory failure, disseminated intravascular coagulation, capillary leak syndrome, and supraventricular and ventricular tachycardia. CRS occurred in 78% of patients in CARTITUDE-4 (3% Grade 3 to 4) and in 95% of patients in CARTITUDE-1 (4% Grade 3 to 4). Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS. Please see Section 5.4; Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS).

Ensure that a minimum of two doses of tocilizumab are available prior to infusion of CARVYKTI®.

Of the 285 patients who received CARVYKTI® in clinical trials, 53% (150/285) patients received tocilizumab; 35% (100/285) received a single dose, while 18% (50/285) received more than 1 dose of tocilizumab. Overall, 14% (39/285) of patients received at least one dose of corticosteroids for treatment of CRS.

Monitor patients at least daily for 10 days following CARVYKTI® infusion at a REMS-certified healthcare facility for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion. At the first sign of CRS, immediately institute treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids.

Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

NEUROLOGIC TOXICITIES, which may be severe, life-threatening, or fatal, occurred following treatment with CARVYKTI®. Neurologic toxicities included ICANS, neurologic toxicity with signs and symptoms of parkinsonism, GBS, immune mediated myelitis, peripheral neuropathies, and cranial nerve palsies. Counsel patients on the signs and symptoms of these neurologic toxicities, and on the delayed nature of onset of some of these toxicities. Instruct patients to seek immediate medical attention for further assessment and management if signs or symptoms of any of these neurologic toxicities occur at any time.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies for RRMM, one or more neurologic toxicities occurred in 24% (69/285), including ≥ Grade 3 cases in 7% (19/285) of patients. Median time to onset was 10 days (range: 1 to 101) with 63/69 (91%) of cases developing by 30 days. Neurologic toxicities resolved in 72% (50/69) of patients with a median duration to resolution of 23 days (range: 1 to 544). Of patients developing neurotoxicity, 96% (66/69) also developed CRS. Subtypes of neurologic toxicities included ICANS in 13%, peripheral neuropathy in 7%, cranial nerve palsy in 7%, parkinsonism in 3%, and immune mediated myelitis in 0.4% of the patients.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Patients receiving CARVYKTI® may experience fatal or life-threatening ICANS following treatment with CARVYKTI®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, ICANS occurred in 13% (36/285), including Grade ≥3 in 2% (6/285) of the patients. Median time to onset of ICANS was 8 days (range: 1 to 28 days). ICANS resolved in 30 of 36 (83%) of patients with a median time to resolution of 3 days (range: 1 to 143 days). Median duration of ICANS was 6 days (range: 1 to 1229 days) in all patients including those with ongoing

neurologic events at the time of death or data cut-off. Of patients with ICANS, 97% (35/36) had CRS. The onset of ICANS occurred during CRS in 69% of patients, before and after the onset of CRS in 14% of patients respectively.

Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS) occurred in 7% of patients in CARTITUDE-4 (0.5% Grade 3) and in 23% of patients in CARTITUDE-1 (3% Grade 3). The most frequent ≥2% manifestations of ICANS included encephalopathy (12%), aphasia (4%), headache (3%), motor dysfunction (3%), ataxia (2%), and sleep disorder (2%) [see Adverse Reactions (6.1)].

Monitor patients at least daily for 10 days following CARVYKTI® infusion at the REMS-certified healthcare facility for signs and symptoms of ICANS. Rule out other causes of ICANS symptoms. Monitor patients for signs or symptoms of ICANS for at least 4 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed [see Dosage and Administration (2.3)].

Parkinsonism: Neurologic toxicity with parkinsonism has been reported in clinical trials of CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, parkinsonism occurred in 3% (8/285), including Grade ≥ 3 in 2% (5/285) of the patients. Median time to onset of parkinsonism was 56 days (range: 14 to 914 days). Parkinsonism resolved in 1 of 8 (13%) of patients with a median time to resolution of 523 days. Median duration of parkinsonism was 243.5 days (range: 62 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cut-off. The onset of parkinsonism occurred after CRS for all patients and after ICANS for 6 patients.

Parkinsonism occurred in 1% of patients in CARTITUDE-4 (no Grade 3 to 4) and in 6% of patients in CARTITUDE-1 (4% Grade 3 to 4).

Manifestations of parkinsonism included movement disorders, cognitive impairment, and personality changes. Monitor patients for signs and symptoms of parkinsonism that may be delayed in onset and managed with supportive care measures. There is limited efficacy information with medications used for the treatment of Parkinson's disease for the improvement or resolution of parkinsonism symptoms following CARVYKTI ® treatment.

Guillain-Barré Syndrome: A fatal outcome following GBS occurred following treatment with CARVYKTI® despite treatment with intravenous immunoglobulins. Symptoms reported include those consistent with Miller-Fisher variant of GBS, encephalopathy, motor weakness, speech disturbances, and polyradiculoneuritis.

Monitor for GBS. Evaluate patients presenting with peripheral neuropathy for GBS. Consider treatment of GBS with supportive care measures and in conjunction with immunoglobulins and plasma exchange, depending on severity of GBS.

Immune Mediated Myelitis: Grade 3 myelitis occurred 25 days following treatment with CARVYKTI® in CARTITUDE-4 in a patient who received CARVYKTI® as subsequent therapy. Symptoms reported included hypoesthesia of the lower extremities and the lower abdomen with impaired sphincter control. Symptoms improved with the use of corticosteroids and intravenous immune globulin. Myelitis was ongoing at the time of death from other cause.

Peripheral Neuropathy occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, peripheral neuropathy occurred in 7% (21/285), including Grade ≥3 in 1% (3/285) of the patients. Median time to onset of peripheral neuropathy was 57 days (range: 1 to 914 days). Peripheral neuropathy resolved in 11 of 21 (52%) of patients with a median time to resolution of 58 days (range: 1 to 215 days). Median duration of peripheral neuropathy was 149.5 days (range: 1 to 692 days) in all patients including those with ongoing neurologic events at the time of death or data cut-off.

Peripheral neuropathies occurred in 7% of patients in CARTITUDE-4 (0.5% Grade 3 to 4) and in 7% of patients in CARTITUDE-1 (2% Grade 3 to 4). Monitor patients for signs and symptoms of peripheral neuropathies. Patients who experience peripheral neuropathy may also experience cranial nerve palsies or GBS.

Cranial Nerve Palsies occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, cranial nerve palsies occurred in 7% (19/285), including Grade ≥3 in 1% (1/285) of the patients. Median time to onset of cranial nerve palsies was 21 days (range: 17 to 101 days). Cranial nerve palsies resolved in 17 of 19 (89%) of patients with a median time to resolution of 66 days (range: 1 to 209 days). Median duration of cranial nerve palsies was 70 days (range: 1 to 262 days) in all patients including those with ongoing neurologic events at the time of death or data cut-off. Cranial nerve palsies occurred in 9% of patients in CARTITUDE-4 (1% Grade 3 to 4) and in 3% of patients in CARTITUDE-1 (1% Grade 3 to 4).

The most frequent cranial nerve affected was the 7th cranial nerve. Additionally, cranial nerves III, V, and VI have been reported to be affected.

Monitor patients for signs and symptoms of cranial nerve palsies. Consider management with systemic corticosteroids, depending on the severity and progression of signs and symptoms.

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)/MACROPHAGE ACTIVATION SYNDROME (MAS): Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, HLH/MAS occurred in 1% (3/285) of patients. All events of HLH/MAS had onset within 99 days of receiving CARVYKTI®, with a median onset of 10 days (range: 8 to 99 days) and all occurred in the setting of ongoing or worsening CRS. The manifestations of HLH/MAS included hyperferritinemia, hypotension, hypoxia with diffuse alveolar damage, coagulopathy and hemorrhage, cytopenia, and multi-organ dysfunction, including renal dysfunction and respiratory failure.

Patients who develop HLH/MAS have an increased risk of severe bleeding. Monitor hematologic parameters in patients with HLH/MAS and transfuse per institutional guidelines. Fatal cases of HLH/MAS occurred following treatment with CARVYKTI®.

HLH is a life-threatening condition with a high mortality rate if not recognized and treated early. Treatment of HLH/MAS should be administered per institutional standards.

CARVYKTI® REMS: Because of the risk of CRS and neurologic toxicities, CARVYKTI® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI® REMS.

Further information is available at https://www.carvyktirems.com or 1-844-672-0067.

PROLONGED AND RECURRENT CYTOPENIAS: Patients may exhibit prolonged and recurrent cytopenias following lymphodepleting chemotherapy and CARVYKTI® infusion. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, Grade 3 or higher cytopenias not resolved by day 30 following CARVYKTI® infusion occurred in 62% (176/285) of the patients and included thrombocytopenia 33% (94/285), neutropenia 27% (76/285), lymphopenia 24% (67/285) and anemia 2% (6/285). After Day 60 following CARVYKTI® infusion 22%, 20%, 5%, and 6% of patients had a recurrence of Grade 3 or 4 lymphopenia, neutropenia, thrombocytopenia, and anemia respectively, after initial recovery of their Grade 3 or 4 cytopenia. Seventy-seven percent (219/285) of patients had one, two, or three or more recurrences of Grade 3 or 4 cytopenias after initial recovery of Grade 3 or 4 cytopenia. Sixteen and 25 patients had Grade 3 or 4 neutropenia and thrombocytopenia, respectively, at the time of death.

Monitor blood counts prior to and after CARVYKTI® infusion. Manage cytopenias with growth factors and blood product transfusion support according to local institutional guidelines.

INFECTIONS: CARVYKTI® should not be administered to patients with active infection or inflammatory disorders. Severe, life-threatening, or fatal infections, occurred in patients after CARVYKTI® infusion.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, infections occurred in 57% (163/285), including ≥Grade 3 in 24% (69/285) of patients. Grade 3 or 4 infections with an unspecified pathogen occurred in 12%, viral infections in 6%, bacterial infections in 5%, and fungal infections in 1% of patients. Overall, 5% (13/285) of patients had Grade 5 infections, 2.5% of which were due to COVID-19. Patients treated with CARVYKTI® had an increased rate of fatal COVID-19 infections compared to the standard therapy arm.

Monitor patients for signs and symptoms of infection before and after CARVYKTI® infusion and treat patients appropriately. Administer prophylactic, pre-emptive, and/or therapeutic antimicrobials according to the standard institutional guidelines. Febrile neutropenia was observed in 5% of patients after CARVYKTI® 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. Counsel patients on the importance of prevention measures. Follow institutional guidelines for the vaccination and management of immunocompromised patients with COVID-19.

Viral Reactivation: Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients with hypogammaglobulinemia. Perform screening for Cytomegalovirus (CMV), HBV, hepatitis C virus (HCV), human immunodeficiency virus (HIV), or any other infectious agents if clinically indicated in accordance with clinical guidelines before collection of cells for manufacturing. Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.

HYPOGAMMAGLOBULINEMIA: can occur in patients receiving treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, hypogammaglobulinemia adverse event was reported in 36% (102/285) of patients; laboratory IgG levels fell below 500mg/dl after infusion in 93% (265/285) of patients.

Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500mg/dl, after infusion occurred in 94% (267/285) of patients treated. Fifty-six percent (161/285) of patients received intravenous immunoglobulin (IVIG) post CARVYKTI® for either an adverse reaction or prophylaxis.

Monitor immunoglobulin levels after treatment with CARVYKTI® and administer IVIG for IgG <400 mg/dL. Manage per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

Use of Live Vaccines: The safety of immunization with live viral vaccines during or following CARVYKTI® 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 CARVYKTI® treatment, and until immune recovery following treatment with CARVYKTI®.

HYPERSENSITIVITY REACTIONS occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, hypersensitivity reactions occurred in 5% (13/285), all of which were ≤ Grade 2. Manifestations of hypersensitivity reactions included flushing, chest discomfort, tachycardia, wheezing, tremor, burning sensation, non-cardiac chest pain, and pyrexia.

Serious hypersensitivity reactions, including anaphylaxis, may be due to the dimethyl sulfoxide (DMSO) in CARVYKTI®. Patients should be carefully monitored for 2 hours after infusion for signs and symptoms of severe reaction. Treat promptly and manage patients appropriately according to the severity of the hypersensitivity reaction.

SECONDARY MALIGNANCIES: Patients treated with CARVYKTI® may develop secondary malignancies. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, myeloid neoplasms occurred in 5% (13/285) of patients (9 cases of myelodysplastic syndrome, 3 cases of acute myeloid leukemia, and 1 case of myelodysplastic syndrome followed by acute myeloid leukemia). The median time to onset of myeloid neoplasms was 447 days (range: 56 to 870 days) after treatment with CARVYKTI®. Ten of these 13 patients died following the development of myeloid neoplasms; 2 of the 13 cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy. Cases of myelodysplastic syndrome and acute myeloid leukemia have also been reported in the post-marketing setting. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T-cell immunotherapies, including CARVYKTI®. Mature T-cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusions and may include fatal outcomes.

Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Janssen Biotech, Inc. at 1-800-526-7736 for reporting and to obtain instructions on collection of patient samples.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Due to the potential for neurologic events, including altered mental status, seizures, neurocognitive decline, or neuropathy, patients receiving CARVYKTI® are at risk for altered or decreased consciousness or coordination in the 8 weeks following CARVYKTI® 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, and in the event of new onset of any neurologic toxicities.

ADVERSE REACTIONS

The most common nonlaboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections-pathogen unspecified, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy, constipation, and vomiting. The most common Grade 3 or 4 laboratory adverse reactions (incidence greater than or equal to 50%) include lymphopenia, neutropenia, white blood cell decreased, thrombocytopenia, and anemia.

Please read full Prescribing Information, including Boxed Warning, for CARVYKTI®.

ABOUT CARVYKTI® (CILTACABTAGENE AUTOLEUCEL; CILTA-CEL)

Ciltacabtagene autoleucel is a BCMA-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T-cells with a transgene encoding a chimeric antigen receptor (CAR) that identifies and eliminates cells that express BCMA. The cilta-cel CAR protein features two BCMA-targeting single domain antibodies designed to confer high avidity against human BCMA. Upon binding to BCMA-expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells.[2]

In December 2017, Legend Biotech entered into an exclusive worldwide license and collaboration agreement with Janssen Biotech, Inc. (Janssen), a Johnson & Johnson company, to develop and commercialize cilta-cel. In February 2022, cilta-cel was approved by the U.S. Food and Drug Administration (FDA) under the brand name CARVYKTI® for the treatment of adults with relapsed or refractory multiple myeloma. In April 2024, cilta-cel was approved for the second-line treatment of patients with relapsed/refractory myeloma who have received at least one prior line of therapy including a proteasome inhibitor, an immunomodulatory agent, and are refractory to lenalidomide.

In May 2022, the European Commission (EC) granted conditional marketing authorization of CARVYKTI® for the treatment of adults with relapsed or refractory multiple myeloma. In September 2022, Japan's Ministry of Health, Labour and Welfare (MHLW) approved CARVYKTI®. Cilta-cel was granted Breakthrough Therapy Designation in the U.S. in December 2019 and in China in August 2020. In addition, cilta-cel received a PRIority MEdicines (PRIME) designation from the European Commission in April 2019. Cilta-cel also received Orphan Drug Designation from the U.S. FDA in February 2019, from the European Commission in February 2020, and from the Pharmaceuticals and Medicinal Devices Agency (PMDA) in Japan in June 2020. In March 2022, the European Medicines Agency's Committee for Orphan Medicinal Products recommended by consensus that the orphan designation for cilta-cel be maintained on the basis of clinical data demonstrating improved and sustained complete response rates following treatment.

ABOUT CARTITUDE-4

CARTITUDE-4 (NCT04181827) is an ongoing, international, randomized, open-label Phase 3 study evaluating the efficacy and safety of cilta-cel versus pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd) in adult patients with relapsed or lenalidomide-refractory multiple myeloma who received one to three prior lines of therapy, including a PI and an IMiD.[3]

ABOUT MULTIPLE MYELOMA

Multiple myeloma is an incurable blood cancer that starts in the bone marrow and is characterized by an excessive proliferation of plasma cells.[4] In 2024, it is estimated that more than 35,000 people will be diagnosed with multiple myeloma, and more than 12,000 people will die from the disease in the U.S.[5] While some patients with multiple myeloma initially have no symptoms, most patients are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[6]

ABOUT LEGEND BIOTECH

Legend Biotech is a global biotechnology company dedicated to treating, and one day curing, life-threatening diseases. Headquartered in Somerset, New Jersey, we are developing advanced cell therapies across a diverse array of technology platforms, including autologous and allogeneic chimeric antigen receptor T-cell, gamma-delta T cell (gd T) and natural killer (NK) cell-based immunotherapy. From our three R&D sites around the world, we apply these innovative technologies to pursue the discovery of cutting-edge therapeutics for patients worldwide.

Learn more at www.legendbiotech.com and follow us on X (formerly Twitter) and LinkedIn.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements in this press release about future expectations, plans, and prospects, as well as any other statements regarding matters that are not historical facts, constitute "forward-looking statements" within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to Legend Biotech's strategies and objectives; statements relating to CARVYKTI ®, including Legend Biotech's expectations for CARVYKTI ® and its therapeutic potential; statements related to the potential results from ongoing studies in the CARTITUDE clinical development program; and the potential benefits of Legend Biotech's product candidates. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. Legend Biotech's expectations could be affected by, among other things, uncertainties involved in the development of new pharmaceutical products; unexpected clinical trial results, including as a result of additional analysis of existing clinical data or unexpected new clinical data; unexpected regulatory actions or delays, including requests for additional safety and/or efficacy data or analysis of data, or government regulation generally; unexpected delays as a result of actions undertaken, or failures to act, by our third party partners; uncertainties arising from challenges to Legend Biotech's patent or other proprietary intellectual property protection, including the uncertainties involved in the U.S. litigation process; government, industry, and general product pricing and other political pressures; as well as the other factors discussed in the "Risk Factors" section of Legend Biotech's Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 19, 2024. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described in this press release as anticipated, believed, estimated or expected. Any forward-looking statements contained in this press release speak only as of the date of this press release. Legend Biotech specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise

‡ Yi Lin, M.D., Ph.D., hematologist and oncologist at Mayo Clinic, Rochester, MN, has provided consulting, advisory, and speaking services to Legend Biotech; has not been paid for any media work.

INVESTOR CONTACT:

Jessie Yeung
Tel: (732) 956-8271
jessie.yeung@legendbiotech.com

PRESS CONTACT:
Mary Ann Ondish
Tel: (914) 552-4625

media@legendbiotech.com

REFERENCES

1 Rakesh Popat et al. Ciltacabtagene Autoleucel (Cilta-cel) Vs Standard of Care (SoC) in Patients with Lenalidomide (Len)-Refractory Multiple Myeloma (MM) after 1-3 Lines of Therapy: Minimal Residual Disease (MRD) Negativity in the Phase 3 Cartitude-4 Trial. American Society of Hematology 2024 Annual Meeting. December 2024

2 CARVYKTI™ Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

3 ClinicalTrials.Gov. A Study Comparing JNJ-68284528, a CAR-T Therapy Directed Against B-cell Maturation Antigen (BCMA), Versus Pomalidomide, Bortezomib and Dexamethasone (PVd) or Daratumumab, Pomalidomide and Dexamethasone (DPd) in Participants With Relapsed and Lenalidomide-Refractory Multiple Myeloma (CARTITUDE-4). https://www.clinicaltrials.gov/study/NCT04181827. Accessed March 2024.

4 American Cancer Society. "What is Multiple Myeloma?". Available at: https://www.cancer.org/cancer/types/multiple-myeloma/about/what-is-multiple-myeloma.html. Accessed March 2024.

5 American Cancer Society. "Key Statistics About Multiple Myeloma." Available at: https://www.cancer.org/cancer/types/multiple-myeloma/about/key-statistics.html. Accessed March 2024

6 American Cancer Society. Multiple myeloma: early detection, diagnosis, and staging. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8740.00.pdf. Accessed March 2023.

Source: Legend Biotech USA Inc.