Genscript Biotech Corporation
金斯瑞生物科技股份有限公司 *
(Incorporated in the Cayman Islands with limited liability)
(Stock code: 1548)

OVERSEAS REGULATORY ANNOUNCEMENT
LEGEND BIOTECH ANNOUNCES RESULTS FROM PHASE 3 CARTITUDE-4 STUDY

This announcement is made by the board of directors (the "**Board**") of Genscript Biotech Corporation (the "**Company**", together with its subsidiaries, the "**Group**") pursuant to Rule 13.10B of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited (the "**Listing Rules**"). Reference is made to the previous announcement of the Company dated 16 May 2023.

Legend Biotech Corporation ("**Legend Biotech**"), a non-wholly owned subsidiary of the Company, whose shares are listed by way of American Depositary Shares on the Nasdaq Global Select Market in the United States (the "**U.S.**"), announced on 5 June 2023 (New York time) that the results from the Phase 3 CARTITUDE-4 study, evaluating ciltacabtagene autoleucel (cilta-cel) for the treatment of adult patients with relapsed and lenalidomide-refractory multiple myeloma who have received one to three prior lines of therapy, demonstrated an improvement in progression-free survival ("**PFS**") compared to standard-of-care ("**SOC**") therapy.

The results from the Phase 3 CARTITUDE-4 study showed that, at a median follow up of 16 months, cilta-cel reduced the risk of disease progression or death by 74 percent compared to standard of care regimens in adult patients with multiple myeloma who have received one to three prior lines of therapy and are refractory to lenalidomide (Hazard ratio [HR]=0.26 (95% CI, 0.18–0.38); P-value [P] <0.0001). The study data were featured in a press briefing and presented in an oral session at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #LBA106) and were presented in the New England Journal of Medicine. On 10 June 2023, results will also be presented in a plenary session at the 2023 European Hematology Association (EHA) Hybrid Congress (Abstract #S100).

Eligible patients in the CARTITUDE-4 study had one to three prior lines of treatment, including proteasome inhibitors (PI) and immunomodulatory drugs and were lenalidomide-refractory. Four hundred and nineteen patients were randomized, with 208 patients in the cilta-cel arm and 211 patients in the SOC arm. At the median follow up of 16 months, the median PFS had not yet been reached in the cilta-cel arm (95% CI, 22.8-NE), compared to a median PFS of 11.8 months in the SOC arm (95%

CI: 9.7, 13.8). In patients who had one prior line of therapy, there was a 65 percent (HR=0.35; 95 percent CI, 0.19-0.66; P<0.0001) reduction in the risk of disease progression or death. Among the secondary endpoints, the overall response rate ("**ORR**") was 85 percent, 73 percent achieved a complete response (CR) or better, and the rate of overall minimal residual disease ("**MRD**") negativity reached 61 percent in the cilta-cel arm. Among patients treated with SOC therapies, the ORR was 67 percent, and 22 percent achieved a CR or better, while 33 percent of patients treated with SOC therapies were MRD negative.

In the study, 97 percent and 94 percent of patients treated in the cilta-cel and SOC groups, respectively, had grade 3 or 4 adverse events, including infections (27 percent versus 25 percent) and cytopenias (94 percent versus 86 percent). Overall, 39 patients in the cilta-cel arm and 46 patients in the SOC arms died, of which 10 cilta-cel and 5 SOC patients passed due to treatment-emergent adverse events (TEAEs). In patients who received cilta-cel as study treatment (n=176), 76 percent had cytokine release syndrome (1 percent grade 3; no grade 4 or 5) and 5 percent had immune effector cell associated neurotoxicity syndrome (all grade 1 or 2). One grade 1 movement and neurocognitive treatment-emergent adverse event was reported in the cilta-cel group.

Final Analysis of CARTITUDE-1 Study Demonstrated Deep and Durable Responses

A final analysis of data from the Phase 1b/2 CARTITUDE-1 (NCT03548207) study showed sustained deep and durable responses in heavily pretreated patients with relapsed or refractory multiple myeloma treated with cilta-cel (Abstract #8009). At a median follow-up of 33.4 months (range, 1.5-45.2), the median PFS was 34.9 months (95 percent CI, 25.2–not estimable [NE]), with an estimated 47.5 percent of patients progression-free and alive at 36 months.

In the study, 97 patients received cilta-cel, with a median of six prior lines of therapy. Forty-two percent of patients were penta-drug refractory, 88 percent were triple-class refractory and 99 percent were refractory to the last line of treatment. At data cut-off, the median duration of response was 33.9 months (95 percent CI, 25.5–NE). Median overall survival ("**OS**") was not reached in the study, with an estimated 62.9 percent OS rate at 36 months. Of 49 MRD-evaluable patients, 26 had MRD-negativity sustained for 12 months or longer, of which 20 had a sustained MRD-negative CR or better. Eighteen patients were MRD-negative with a CR or better at 24-months post infusion. No new safety signals and no new neurotoxicity events were reported since the 27.7-month median follow-up. Six new cases of second primary malignancy were reported, including two cases of basal cell carcinoma and one case each of myelodysplastic syndrome, B-cell lymphoma, melanoma and prostate cancer. Five additional deaths occurred in the study (PD, n=3; pneumonia and sepsis, n=1 each, both determined by the investigators to be unrelated to cilta-cel), for a total of 35 deaths in the study (PD, n=17; unrelated to cilta-cel, n=12; related, n=6, as determined by investigators).

Five-Year Follow-up Data from LEGEND-2 Highlights Sustained, Durable Responses

Five-year follow-up data from LEGEND-2, the longest follow-up for any BCMA-targeted CAR-T cell therapy study investigating LCAR-B38M, a similar CAR construct to cilta-cel, showed a median OS of 55.8 months, with 18 percent of patients with heavily pretreated multiple myeloma remaining disease-free.

At the data cut-off, median follow-up in the LEGEND-2 study was 65.4 months (range, 0.4-78.8). Seventy-four patients received LCAR-B38M, with a median of three prior lines of therapy (range, 1-

9); 35.7 percent of patients had high risk cytogenic profiles. In the study, the ORR was 87.8 percent, and 73 percent of patients achieved a CR. The median duration of response in the study was 23 months, and median PFS was 18 months at maturity, consistent with previously reported data. The rate of MRD-negative CR was 67.6 percent. No new CAR-T cell-related toxicities were reported in the analysis.

For details of the indications and usage, important safety information and warnings and precautions of CARVYKTI®, please refer to the attached Form 6-K and its exhibit. The attachment is the full Form 6-K and its exhibit as published on the SEC's website available at https://investors.legendbiotech.com/static-files/fd422b67-2c55-4138-b3b2-7b85569cd5c7.

Legend Biotech hosted an investor event (the "**Investor Event**") to present this data at 7 am on 5 June 2023 (Central time), which was also available for participation via webcast on Legend Biotech's investor relations site under events and presentations at https://investors.legendbiotech.com/events-and-presentations.

Cautionary Note Regarding Forward-Looking Statements

Statements in the attached Form 6-K and its exhibit 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® and any other product candidates, including Legend Biotech's expectations for CARVYKTI® and any other product candidates, such as Legend Biotech's manufacturing and commercialization expectations for CARVYKTI® and the potential effect of treatment with CARVYKTI® and any other product candidates; statements about submissions for CARVYKTI® and any other product candidates, and the progress of such submissions with the U.S. FDA and other regulatory authorities; the anticipated timing of, and ability to progress, clinical trials; the ability to generate, analyze and present data from clinical trials; expected results of clinical trials; 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; competition in general; government, industry, and general product pricing and other political pressures; the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation; 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 SEC on 30 March 2023. 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 the attached Form 6-K and its exhibit as anticipated, believed,

estimated or expected. Any forward-looking statements contained in the attached Form 6-K and its exhibit speak only as of the date of the attached Form 6-K. The Group and Legend Biotech specifically disclaim any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

Shareholders and potential investors of the Company are advised to pay attention to investment risks and exercise caution when they deal or contemplate dealing in the securities of the Company.

By Order of the Board
Genscript Biotech Corporation
MENG Jiange
Chairman and Executive Director

Hong Kong, 6 June 2023

As at the date of this announcement, the executive Directors are Dr. Zhang Fangliang, Mr. Meng Jiange, Ms. Wang Ye and Dr. Zhu Li; the non-executive Directors are Dr. Wang Luquan, Mr. Pan Yuexin and Ms. Wang Jiafen; and the independent non-executive Directors are Mr. Guo Hongxin, Mr. Dai Zumian, Mr. Pan Jiuan and Dr. Wang Xuehai

* *For identification purposes only*

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 6-K

Report of Foreign Private Issuer
Pursuant to Rule 13a-16 or 15d-16
of the Securities Exchange Act of 1934

Date of Report: June 5, 2023

Commission File Number: 001-39307

Legend Biotech Corporation
(Exact Name of Registrant as Specified in its Charter)

2101 Cottontail Lane
Somerset, New Jersey 08873
(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

Legend Biotech Announces Results from Phase 3 CARTITUDE-4 study, evaluating ciltacabtagene autoleucel (cilta-cel) for the treatment of adult patients with relapsed and lenalidomide-refractory multiple myeloma

On June 5, 2023, Legend Biotech Corporation ("Legend Biotech" or the "Company") issued a press release announcing that the results from the Phase 3 CARTITUDE-4 study, evaluating ciltacabtagene autoleucel (cilta-cel) for the treatment of adult patients with relapsed and lenalidomide-refractory multiple myeloma who have received one to three prior lines of therapy, demonstrated an improvement in progression-free survival (PFS) compared to standard-of-care (SOC) therapy, which is attached to this Form 6-K as Exhibit 99.1 and is incorporated herein by reference.

The Company also hosted an investor event to present this data at 7am Central Time on June 5, 2023, which was also available for participation via webcast on the Company's investor relations site under events and presentations: https://investors.legendbiotech.com/events-and-presentations.

This report on Form 6-K, including Exhibit 99.1, is hereby incorporated by reference in the registration statements of Legend Biotech on Form F-3 (Nos. 333-272222, 333-257609 and 333-257625) and Form S-8 (No. 333-239478), to the extent not superseded by documents or reports subsequently filed.

EXHIBIT INDEX

Exhibit	Title
99.1	Press Release, dated June 5, 2023

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

LEGEND BIOTECH CORPORATION

Date: June 5, 2023

By: /s/ Ying Huang
Name: Ying Huang, Ph.D.
Title: Chief Executive Officer

Ciltacabtagene Autoleucel (cilta-cel) Reduced Risk of Disease Progression or Death by 74% vs Standard Regimens for Adult Patients with Relapsed and Refractory Multiple Myeloma in CARTITUDE-4 Study

June 5, 2023

- *First analysis data from CARTITUDE-4 demonstrated a statistically significant improvement in progression-free survival, with a hazard ratio of 0.26*
- *CARTITUDE-4 is the first randomized study investigating the efficacy of a cell therapy versus standard of care (DPd or PVd) as early as after first relapse in lenalidomide-refractory multiple myeloma*
- *Long-term results from CARTITUDE-1 and LEGEND-2 demonstrated sustained deep and durable responses*

SOMERSET, N.J.--(BUSINESS WIRE)--Jun. 5, 2023-- Legend Biotech Corporation (NASDAQ: LEGN) (Legend Biotech), a global biotechnology company developing, manufacturing and commercializing novel therapies to treat life-threatening diseases, announced today that results from the Phase 3 CARTITUDE-4 study showed that, at a median follow up of 16 months, cilta-cel reduced the risk of disease progression or death by 74 percent compared to standard of care regimens in adult patients with multiple myeloma who have received one to three prior lines of therapy and are refractory to lenalidomide (Hazard ratio [HR]=0.26 (95% CI, 0.18–0.38); P-value [P] <0.0001).[1] The study data were featured in a press briefing and presented in an oral session at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #LBA106) and were presented in the *New England Journal of Medicine.* On Saturday, June 10, 2023, results will also be presented in a plenary session at the 2023 European Hematology Association (EHA) Hybrid Congress (Abstract #S100).

Eligible patients in the CARTITUDE-4 study had one to three prior lines of treatment, including proteasome inhibitors (PI) and immunomodulatory drugs and were lenalidomide-refractory.[1] Four hundred and nineteen patients were randomized, with 208 patients in the cilta-cel arm and 211 patients in the SOC arm. At the median follow up of 16 months, the median PFS had not yet been reached in the cilta-cel arm (95% CI, 22.8-NE), compared to a median PFS of 11.8 months in the SOC arm (95% CI: 9.7-13.8). In patients who had one prior line of therapy, there was a 65 percent (HR=0.35; 95 percent CI, 0.19-0.66; P<0.0001) reduction in the risk of disease progression or death. Among the secondary endpoints, the overall response rate (ORR) was 85 percent, 73 percent achieved a complete response (CR) or better, and the rate of overall minimal residual disease (MRD) negativity reached 61 percent in the cilta-cel arm.[1] Among patients treated with SOC therapies, the ORR was 67 percent, and 22 percent achieved a CR or better, while 33 percent of patients treated with SOC therapies were MRD negative.[1]

“There continues to be a serious unmet need in multiple myeloma, particularly in earlier lines of treatment,” said Binod Dhakal, M.D., M.S., Associate Professor of Medicine at the Medical College of Wisconsin, Division of Hematology, and study investigator. “The CARTITUDE-4 results demonstrate the potential for cilta-cel to be an additional treatment option for appropriate patients with relapsed and refractory multiple myeloma who have had one to three prior lines of therapy.”

In the study, 97 percent and 94 percent of patients treated in the cilta-cel and SOC groups, respectively, had grade 3 or 4 adverse events, including infections (27 percent versus 25 percent) and cytopenias (94 percent versus 86 percent).[1] Overall, 39 patients in the cilta-cel arm and 46 patients in the SOC arms died, of which 10 cilta-cel and 5 SOC patients passed due to treatment-emergent adverse events (TEAEs).[1] In patients who received cilta-cel as study treatment (n=176), 76 percent had cytokine release syndrome (1 percent grade 3; no grade 4 or 5) and 5 percent had immune effector cell associated neurotoxicity syndrome (all grade 1 or 2).[1] One grade 1 movement and neurocognitive treatment-emergent adverse event was reported in the cilta-cel group.[1]

“Data from CARTITUDE-4 demonstrated strong results for study patients after first relapse,” said Mythili Koneru, M.D., Chief Medical Officer at Legend Biotech. “We are inspired by the potential of cilta-cel for patients with multiple myeloma who continue to have a high need for another treatment option.”

Final Analysis of CARTITUDE-1 Study Demonstrated Deep and Durable Responses

A final analysis of data from the Phase 1b/2 CARTITUDE-1 (NCT03548207) study showed sustained deep and durable responses in heavily pretreated patients with relapsed or refractory multiple myeloma treated with cilta-cel (Abstract #8009).[2] At a median follow-up of 33.4 months (range, 1.5-45.2), the median PFS was 34.9 months (95 percent CI, 25.2–not estimable [NE]), with an estimated 47.5 percent of patients progression-free and alive at 36 months.[2]

In the study, 97 patients received cilta-cel, with a median of six prior lines of therapy.[2] Forty-two percent of patients were penta-drug refractory, 88 percent were triple-class refractory and 99 percent were refractory to the last line of treatment.[2] At data cut-off, the median duration of response was 33.9 months (95 percent CI, 25.5–NE).[2] Median overall survival (OS) was not reached in the study, with an estimated 62.9 percent OS rate at 36 months.[2] Of 49 MRD-evaluable patients, 26 had MRD-negativity sustained for 12 months or longer, of which 20 had a sustained MRD-negative CR or better.[2] Eighteen patients were MRD-negative with a CR or better at 24-months post infusion.[2] No new safety signals and no new neurotoxicity events were reported since the 27.7-month median follow-up.[2] Six new cases of second primary malignancy were reported, including two cases of basal cell carcinoma and one case each of myelodysplastic syndrome, B-cell lymphoma, melanoma and prostate cancer.[2] Five additional deaths occurred in the

study (PD, n=3; pneumonia and sepsis, n=1 each, both determined by the investigators to be unrelated to cilta-cel), for a total of 35 deaths in the study (PD, n=17; unrelated to cilta-cel, n=12; related, n=6, as determined by investigators).[2]

Five-Year Follow-up Data from LEGEND-2 Highlights Sustained, Durable Responses

Five-year follow-up data from LEGEND-2, the longest follow-up for any BCMA-targeted CAR-T cell therapy study investigating LCAR-B38M, a similar CAR construct to cilta-cel, showed a median OS of 55.8 months, with 18 percent of patients with heavily pretreated multiple myeloma remaining disease-free.[3]

At the data cut-off, median follow-up in the LEGEND-2 study was 65.4 months (range, 0.4-78.8).[3] Seventy-four patients received LCAR-B38M, with a median of three prior lines of therapy (range, 1-9); 35.7 percent of patients had high risk cytogenic profiles.[3] In the study, the ORR was 87.8 percent, and 73 percent of patients achieved a CR.[3] The median duration of response in the study was 23 months, and median PFS was 18 months at maturity, consistent with previously reported data.[3] The rate of MRD-negative CR was 67.6 percent.[3] No new CAR-T cell-related toxicities were reported in the analysis.[3]

Disclosure: Dr. Dhakal has provided consulting, advisory, and speaking services to Legend Biotech and Janssen Biotech, Inc.

CARVYKTI® Important Safety Information

CARVYKTI® INDICATIONS AND USAGE

CARVYKTI® (ciltacabtagene autoleucel) is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma, after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

CARVYKTI® IMPORTANT SAFETY INFORMATION

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

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 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®.

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

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS) including fatal or life-threatening reactions, occurred following treatment with CARVYKTI® in 95% (92/97) of patients receiving ciltacabtagene autoleucel. Grade 3 or higher CRS (2019 ASTCT grade) occurred in 5% (5/97) of patients, with Grade 5 CRS reported in 1 patient. The median time to onset of CRS was 7 days (range: 112 days). The most common manifestations of CRS included pyrexia (100%), hypotension (43%), increased aspartate aminotransferase (AST) (22%), chills (15%), increased alanine aminotransferase (ALT) (14%) and sinus tachycardia (11%). Grade 3 or higher events associated with CRS included increased AST and ALT, hyperbilirubinemia, hypotension, pyrexia, hypoxia, respiratory failure, acute kidney injury, disseminated intravascular coagulation, HLH/MAS, angina pectoris, supraventricular and ventricular tachycardia, malaise, myalgias, increased C-reactive protein, ferritin, blood alkaline phosphatase and gamma-glutamyl transferase.

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.

Sixty-nine of 97 (71%) patients received tocilizumab and/or a corticosteroid for CRS after infusion of ciltacabtagene autoleucel. Forty-four (45%) patients received only tocilizumab, of whom 33 (34%) received a single dose and 11 (11%) received more than one dose; 24 patients (25%) received tocilizumab and a corticosteroid, and one patient (1%) received only corticosteroids. Ensure that a minimum of two doses of tocilizumab are available prior to infusion of CARVYKTI®.

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, Guillain-Barré Syndrome, 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.

Overall, one or more subtypes of neurologic toxicity described below occurred following ciltacabtagene autoleucel in 26% (25/97) of patients, of which 11% (11/97) of patients experienced Grade 3 or higher events. These subtypes of neurologic toxicities were also observed in two ongoing studies.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Patients 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. ICANS occurred in 23% (22/97) of patients receiving ciltacabtagene autoleucel including Grade 3 or 4 events in 3% (3/97) and Grade 5 (fatal) events in 2% (2/97). The median time to onset of ICANS was 8 days (range 1-28 days). All 22 patients with ICANS had CRS. The most frequent (≥5%) manifestation of ICANS included encephalopathy (23%), aphasia (8%) and headache (6%).

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.

Parkinsonism: Of the 25 patients in the CARTITUDE-1 study experiencing any neurotoxicity, five male patients had neurologic toxicity with several signs and symptoms of parkinsonism, distinct from immune effector cell-associated neurotoxicity syndrome (ICANS). Neurologic toxicity with parkinsonism has been reported in other ongoing trials of ciltacabtagene autoleucel. Patients had parkinsonian and non-parkinsonian symptoms that included tremor, bradykinesia, involuntary movements, stereotypy, loss of spontaneous movements, masked facies, apathy, flat affect, fatigue, rigidity, psychomotor retardation, micrographia, dysgraphia, apraxia, lethargy, confusion, somnolence, loss of consciousness, delayed reflexes, hyperreflexia, memory loss, difficulty swallowing, bowel incontinence, falls, stooped posture, shuffling gait, muscle weakness and wasting, motor dysfunction, motor and sensory loss, akinetic mutism, and frontal lobe release signs. The median onset of parkinsonism in the 5 patients in CARTITUDE-1 was 43 days (range 15-108) from infusion of ciltacabtagene autoleucel.

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 Guillain-Barré Syndrome (GBS) has occurred in another ongoing study of ciltacabtagene autoleucel 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.

Peripheral Neuropathy: Six patients in CARTITUDE-1 developed peripheral neuropathy. These neuropathies presented as sensory, motor or sensorimotor neuropathies. Median time of onset of symptoms was 62 days (range 4-136 days), median duration of peripheral neuropathies was 256 days (range 2-465 days) including those with ongoing neuropathy. Patients who experienced peripheral neuropathy also experienced cranial nerve palsies or GBS in other ongoing trials of ciltacabtagene autoleucel.

Cranial Nerve Palsies: Three patients (3.1%) experienced cranial nerve palsies in CARTITUDE1. All three patients had 7th cranial nerve palsy; one patient had 5th cranial nerve palsy as well. Median time to onset was 26 days (range 21-101 days) following infusion of ciltacabtagene autoleucel. Occurrence of 3rd and 6th cranial nerve palsy, bilateral 7th cranial nerve palsy, worsening of cranial nerve palsy after improvement, and occurrence of peripheral neuropathy in patients with cranial nerve palsy have also been reported in ongoing trials of ciltacabtagene autoleucel. 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): Fatal HLH occurred in one patient (1%), 99 days after ciltacabtagene autoleucel. The HLH event was preceded by prolonged CRS lasting 97 days. The manifestations of HLH/MAS include hypotension, hypoxia with diffuse alveolar damage, coagulopathy, cytopenia, and multi-organ dysfunction, including renal dysfunction. 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 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. One patient underwent autologous stem cell therapy for hematopoietic reconstitution due to prolonged thrombocytopenia.

In CARTITUDE-1, 30% (29/97) of patients experienced prolonged Grade 3 or 4 neutropenia and 41% (40/97) of patients experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Day 30 following ciltacabtagene autoleucel infusion.

Recurrent Grade 3 or 4 neutropenia, thrombocytopenia, lymphopenia and anemia were seen in 63% (61/97), 18% (17/97), 60% (58/97), and 37% (36/97) after recovery from initial Grade 3 or 4 cytopenia following infusion. After Day 60 following ciltacabtagene autoleucel infusion, 31%, 12% and 6% of patients had a recurrence of Grade 3 or higher lymphopenia, neutropenia and thrombocytopenia, respectively, after initial recovery of their Grade 3 or 4 cytopenia. Eighty-seven percent (84/97) 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. Six and 11 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.

Infections (all grades) occurred in 57 (59%) patients. Grade 3 or 4 infections occurred in 23% (22/97) of patients; Grade 3 or 4 infections with an unspecified pathogen occurred in 17%, viral infections in 7%, bacterial infections in 1%, and fungal infections in 1% of patients. Overall, four patients had Grade 5 infections: lung abscess (n=1), sepsis (n=2) and pneumonia (n=1).

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 10% of patients after ciltacabtagene autoleucel 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 with hypogammaglobulinemia. Perform screening for Cytomegalovirus (CMV), HBV, hepatitis C virus (HCV), and 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 was reported as an adverse event in 12% (12/97) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 92% (89/97) of patients. 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 have occurred in 5% (5/97) of patients following ciltacabtagene autoleucel infusion. 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 appropriately according to the severity of the hypersensitivity reaction.

Secondary Malignancies: Patients may develop secondary malignancies. 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 for testing of secondary malignancy of T cell origin.

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 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 non-laboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections of unspecified pathogen, 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 laboratory adverse reactions (incidence greater than or equal to 50%) include thrombocytopenia, neutropenia, anemia, aminotransferase elevation, and hypoalbuminemia.

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. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B-cells and plasma cells. 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.[4]

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.[5] In May 2022, the European Commission (EC) granted conditional marketing authorization of CARVYKTI® for the treatment of adults with relapsed and refractory multiple myeloma.[6] In September 2022, Japan's Ministry of Health, Labour and Welfare (MHLW) approved CARVYKTI®.[7] 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.[8]

In December 2017, Legend Biotech entered into an exclusive worldwide license and collaboration agreement with Janssen Biotech, Inc. (Janssen) to develop and commercialize cilta-cel.

About CARTITUDE-4

CARTITUDE-4 (NCT04181827) is the first international, randomized, open-label Phase 3 study evaluating the efficacy and safety of a CAR-T therapy versus pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd) in adult patients with relapsed and lenalidomide-refractory multiple myeloma who received one to three prior lines of therapy. After apheresis, patients randomized to the cilta-cel arm of the study received either PVd or DPd as bridging therapy, followed by an infusion of cilta-cel five to seven days after lymphodepletion. In total, 176 patients received planned cilta-cel treatment and 20 received cilta-cel after disease progression during bridging therapy.[1] In the SOC group, 28 patients were treated with PVd and 183 patients were treated with DPd until disease progression.[1] The primary endpoint of the study is PFS. Secondary endpoints include safety, overall survival (OS), minimal residual disease (MRD) negative rate and overall response rate (ORR). Patients will continue to be followed for primary and secondary endpoints as part of the CARTITUDE-4 study.

About CARTITUDE-1

CARTITUDE-1 (NCT03548207) is a Phase 1b/2, open-label, single arm, multi-center trial evaluating cilta-cel for the treatment of adult patients with relapsed or refractory multiple myeloma, who previously received at least three prior lines of therapy including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 monoclonal antibody. Of the 97 patients enrolled in the trial, 99 percent were refractory to the last line of treatment and 88 percent were triple-class refractory, meaning their cancer did not respond, or no longer responds, to an IMiD, a PI and an anti-CD38 monoclonal antibody.

About LEGEND-2

LEGEND-2 (NCT03090659) is a Phase 1/2, single-arm, open-label program in China comprised of four independent institutional studies conducted at participating hospitals evaluating the efficacy and safety of LCAR-B38M for the treatment of patients with R/R multiple myeloma. LCAR-B38M identifies the investigational product being studied in China and Ciltacabtagene autoleucel (cilta-cel) identifies the investigational product being studied in the U.S./EU, both of which are representative of the same CAR-T therapy.

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.[9] In 2023, 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.[10] While some patients with multiple myeloma have no symptoms at all, most patients are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[11] Although treatment may result in remission, unfortunately, patients will most likely relapse.[12] Patients who relapse after treatment with standard therapies, including protease inhibitors, immunomodulatory agents, and an anti-CD38 monoclonal antibody, have poor prognoses and few treatment options available.[13,14]

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 (γδ 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 safe, efficacious and cutting-edge therapeutics for patients worldwide.

Learn more at www.legendbiotech.com and follow us on 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 ® and any other product candidates, including Legend Biotech's expectations for CARVYKTI ® and any other product candidates, such as the potential effect of treatment with CARVYKTI® and any other product candidates; the anticipated timing of, and ability to progress, clinical trials; the ability to generate, analyze and present data from clinical trials; expected results of clinical trials; 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; competition in general; government, industry, and general product pricing and other political pressures; the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation; 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 30, 2023. 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.

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