



Legend Biotech Announces Phase 1b/2 Study Data of Cilta-cel, an Investigational BCMA CAR-T, Showing Early, Deep, and Durable Responses in Heavily Pretreated Patients with Multiple Myeloma

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Combined Phase 1b/2 CARTITUDE-1 study presented at ASH 2020 Annual Meeting show 97 percent overall response rate and 12-month progression free survival rate of 77 percent at median follow up of 12.4 months

SOMERSET, N.J.--(BUSINESS WIRE)--Dec. 5, 2020-- Legend Biotech Corporation (NASDAQ: LEGN) ("Legend Biotech"), a global clinical-stage biopharmaceutical company engaged in the discovery and development of novel cell therapies for oncology and other indications, today announced the latest data results from the combined Phase 1b/2 CARTITUDE-1 study ([NCT03548207](#)) of ciltacabtagene autoleucel (cilta-cel), an investigational B-cell maturation antigen (BCMA) directed chimeric antigen receptor T cell (CAR-T) therapy, for the treatment of patients with relapsed or refractory multiple myeloma (RRMM), sponsored by Janssen Research & Development, LLC. The data continued to show a very high overall response rate (ORR) that deepened over time, with 97 percent of patients achieving a response and 67 percent of patients achieving a stringent complete response (sCR) at a median follow-up of 12.4 months.¹ The data were presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition ([Abstract #177](#)) as an oral presentation.

"A 97 percent response rate is extraordinary when you consider the patient population who, prior to cilta-cel, have generally experienced low response rates," said Deepu Madduri, M.D., Assistant Professor of Medicine, Hematology and Medical Oncology, Tisch Cancer Institute at Mount Sinai, New York, and principal CARTITUDE-1 study investigator. "Considering the early, deep and durable responses that we've seen at low-dose infusion of cilta-cel and its manageable safety profile, we look forward to further studying outpatient administration of cilta-cel in patients with multiple myeloma in earlier settings."

The trial included 97 patients treated with cilta-cel who received a median of six (range, 3-18) prior lines of therapy; 88 percent (n=85) were triple-refractory, 42 percent (n=41) were penta-refractory and 99 percent (n=96) were refractory to the last line of therapy.¹ The median administered dose was 0.71×10^6 CAR+ viable T cells/kg and manufacturing of cilta-cel was successful for all patients. ORR per independent review was 97 percent, which included a sCR rate of 67 percent, very good partial response rate (VGPR) of 26 percent (VGPR or better, 93 percent) and partial response rate of 4 percent. Median time to first response was 1 month (range, 0.9-8.5) and responses were ongoing in 72 percent (n=70) of patients. Of 57 minimal residual disease (MRD) evaluable patients, 93 percent (n=53) were MRD negative at 10^{-5} .¹ Median progression-free survival (PFS) was not reached at median follow-up of 12.4 months (range, 1.5-24.9). The 12-month PFS rate was 77 percent (95 percent confidence interval [CI], 66-84) and the 12-month OS rate was 89 percent (95 percent CI, 80-94).¹

The study also demonstrated a manageable safety profile for cilta-cel at the recommended Phase 2 dose.¹ In the combined results, the most common hematologic adverse events (AEs) observed in the CARTITUDE-1 study were neutropenia (96 percent); anemia (81 percent); thrombocytopenia (79 percent); leukopenia (62 percent); and lymphopenia (53 percent).¹ Cytokine release syndrome (CRS) of any grade was observed in 95 percent of patients, with a median duration of four days (range, 1-97), and 99 percent of which resolved within 14 days of onset. Of the 92 patients with CRS, most were Grade 1/2 (95 percent, n=87), 3 percent were Grade 3 (n=3), 1 percent was Grade 4 (n=1) and 1 percent was Grade 5 (n=1).¹ The median onset of CRS was seven days (range, 1-12) post-infusion, with 89 percent (n=82) of patients experiencing CRS onset at day four or later, which is supportive of potential outpatient administration for cilta-cel. Total CAR-T cell neurotoxicity of any grade was observed in 21 percent (n=20) of patients, with Grade ≥ 3 neurotoxicity observed in 10 percent (n=10) of patients.¹ Of these, Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS) was observed in 16 patients and generally occurred concurrently with CRS; other neurotoxicities were observed in 12 patients and generally occurred after resolution of CRS and/or ICANS (eight patients experienced both ICANS and other neurotoxicities).¹ ICANS events were resolved in all patients with a median time to recovery of four days (range, 1-12).¹ Other neurotoxicities were resolved in six patients at a median time of 75 days (range, 2-160) and were not resolved in six patients (one with ongoing toxicity, one died from neurotoxicity and four died due to other causes).¹ Fourteen deaths were reported during the study: five due to disease progression, three due to adverse events unrelated to treatment (acute myelogenous leukemia [n=2], pneumonia [n=1]) and six due to adverse events related to treatment (sepsis and/or septic shock [n=2], CRS/HLH [n=1], neurotoxicity [n=1], respiratory failure [n=1], and lung abscess [n=1]).¹

"We are encouraged by the see strong results from the CARTITUDE-1 study showing the potential of our lead product candidate cilta-cel to be a transformative treatment option for patients living with relapsed or refractory multiple myeloma," said Dr. Ying Huang, Chief Executive Officer and Chief Financial Officer of Legend Biotech. "We look forward to advancing this potentially life-saving treatment approach for patients in need."

About CARTITUDE-1

CARTITUDE-1 ([NCT03548207](#)) is an ongoing Phase 1b/2, open-label, multicenter study evaluating the safety and efficacy of ciltacabtagene autoleucel in adults with relapsed or refractory multiple myeloma, 99 percent of whom were refractory to the last line of treatment; 88 percent of whom were triple-class refractory (to at least 1 immunomodulatory drug [IMiD], 1 proteasome inhibitor [PI] and 1 anti-CD38 antibody).

The primary objective of the Phase 1b portion of the study, involving 29 patients, was to characterize the safety and confirm the dose of ciltacabtagene autoleucel, informed by the first-in-human study with LCAR-B38M CAR-T cells (LEGEND-2). The Phase 2 portion of the study, involving 68 additional patients, is evaluating the efficacy of ciltacabtagene autoleucel with overall response rate as the primary endpoint.

About Cilta-cel

Cilta-cel is an investigational chimeric antigen receptor T (CAR-T) cell therapy, formerly identified as JNJ-4528 outside of China and LCAR-B38M CAR-T cells in China, that is being studied in a comprehensive clinical development program for the treatment of patients with relapsed or refractory multiple myeloma and in earlier lines of treatment. The design consists of a structurally differentiated CAR-T with two BCMA-targeting single domain antibodies. In December 2017, Legend Biotech, Inc. entered into an exclusive worldwide license and collaboration agreement with Janssen Biotech, Inc. (Janssen) to develop and commercialize cilta-cel. In addition to a Breakthrough Therapy Designation (BTD) granted in the U.S. in December 2019, cilta-cel received a PRiority MEdicines (PRIME) designation from the European Commission in April 2019 and BTD in China in August 2020. In addition, Orphan Drug Designation was granted for cilta-cel by the U.S. FDA in February 2019, and by the European Commission in February 2020.

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.² Although treatment may result in remission, unfortunately, patients will most likely relapse.³ Relapsed myeloma is when the disease has returned after a period of initial, partial or complete remission and does not meet the definition of being refractory.⁴ Refractory multiple myeloma is when a patient's disease is non-responsive or progresses within 60 days of their last therapy.^{5,6} While some patients with multiple myeloma have no symptoms until later stages of the disease, most patients are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.⁷ Patients who relapse after treatment with standard therapies, including protease inhibitors and immunomodulatory agents, have poor prognoses and few treatment options.⁸

About Legend Biotech

Legend Biotech is a global clinical-stage biopharmaceutical company engaged in the discovery and development of novel cell therapies for oncology and other indications. Our team of over 800 employees across the United States, China and Europe, along with our differentiated technology, global development, and manufacturing strategies and expertise, provide us with the strong potential to discover, develop, and manufacture cutting-edge cell therapies for patients in need. We are engaged in a strategic collaboration to develop and commercialize our lead product candidate, ciltacabtagene autoleucel, an investigational BCMA targeted CAR-T cell therapy for patients with multiple myeloma. This candidate is currently being studied in registrational clinical trials. To learn more about Legend Biotech, visit us on LinkedIn, or on Twitter @LegendBiotech or at www.legendbiotech.com.

Cautions Concerning 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, may 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 clinical efforts, its collaboration to develop and commercialize cilta-cel, and the data relating to the CARTITUDE-1 study. 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, including the factors discussed in the "Risk Factors" section of the prospectus filed with the Securities and Exchange Commission on June 8, 2020. Any forward-looking statements contained in this press release speak only as of the date hereof, and Legend Biotech specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise. Readers should not rely upon the information on this page as current or accurate after its publication date.

The safety and efficacy of the product candidates and/or uses under investigation have not been established. There is no guarantee that the product candidates will receive health authority approval or become commercially available in any country for the uses being investigated.

¹ Madduri, D et al. Cartitude-1: Phase 1b/2 Study of Ciltacabtagene Autoleucel, a B-Cell Maturation Antigen-Directed Chimeric Antigen Receptor T Cell Therapy, in Relapsed/Refractory Multiple Myeloma. Abstract #177. Oral Presentation at 2020 American Society of Hematology Annual Meeting.

² American Society of Clinical Oncology. Multiple myeloma: introduction. Available at: <https://www.cancer.net/cancer-types/multiple-myeloma/introduction>. Accessed November 2020.

³ Abdi J, Chen G, Chang H, et al. Drug resistance in multiple myeloma: latest findings and new concepts on molecular mechanisms. *Oncotarget*. 2013;4:2186-2207.

⁴ National Cancer Institute. NCI dictionary of cancer terms: relapsed. Available at: <https://www.cancer.gov/publications/dictionaries/cancer-terms?CdrID=45866>. Accessed November 2020.

⁵ National Cancer Institute. NCI dictionary of cancer terms: refractory. Available at: <https://www.cancer.gov/publications/dictionaries/cancer-terms?CdrID=350245>. Accessed November 2020.

⁶ Richardson P, Mitsiades C, Schlossman R, et al. The treatment of relapsed and refractory multiple myeloma. *Hematology Am Soc Hematol Educ Program*. 2007:317-23.

⁷ 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 November 2020.

⁸ Kumar SK, Lee JH, Lahuerta JJ, et al. Risk of progression and survival in multiple myeloma relapsing after therapy with IMiDs and bortezomib: a multicenter international myeloma working group study. *Leukemia*. 2012;26:149-57.

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