Two-Year Analysis of CARTITUDE-1 Shows Early, Durable and Deepening Responses of Ciltacabtagene Autoleucel (cilta-cel) in Heavily Pretreated Patients with Multiple Myeloma

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- Updated CARTITUDE-1 data presented at ASH 2021 demonstrate a 98 percent overall response rate and 83 percent stringent complete response rate after nearly two years of follow-up
- CARTITUDE-1 study data also reported 2-year progression-free survival and overall survival rates were 61 and 74 percent, respectively
- New results from CARTITUDE-2 study of cilta-cel in earlier lines of treatment were also presented at ASH, including first data from Cohort B and longer-term data from Cohort A

SOMERSET, N.J.--(BUSINESS WIRE)--Dec. 13, 2021-- Legend Biotech Corporation (NASDAQ: LEGN) (Legend Biotech), a global, clinical-stage biotechnology company developing and manufacturing novel therapies, announced today new and updated results from the CARTITUDE clinical development program studying ciltacabtagene autoleucel (cilta-cel) in the treatment of multiple myeloma, which were presented at the 63rd American Society of Hematology (ASH) Annual Meeting and Exposition. Cilta-cel is an investigational B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T cell (CAR-T) therapy being studied as a one-time treatment for multiple myeloma.

CARTITUDE-1 Data Continues to Support the Potential of Cilta-cel

In an oral presentation (Abstract #549), longer-term results from the Phase 1b/2 CARTITUDE-1 study in 97 patients with relapsed or refractory multiple myeloma (RRMM) continued to show a very high overall response rate (ORR) of 98 percent. After 21.7 months of follow-up, 83 percent of patients treated with cilta-cel achieved a stringent complete response (sCR)—higher than the 67 percent sCR rate reported at a median of ~1 year of follow up.[1] Further, 95 percent of patients achieved a very good partial response (VGPR) or better. Median progression-free survival (PFS) and median overall survival (OS) have not been reached, but the 2-year PFS rate was 61 percent (95 percent Confidence Interval [CI], 48.5–70.4) and the 2-year OS rate was 74 percent (95 percent CI, 61.9–82.7). Of the 61 patients evaluable for minimal residual disease (MRD), 92 percent were MRD-negative at the 10^{-5} cutoff threshold. The two-year PFS rates in patients with sustained MRD negativity for ≥6 and ≥12 months were 91 percent (95 percent CI, 67.1–97.8) and 100 percent, respectively.

The median time to first response was one month (range, 0.9-10.7); the median time to best response was 2.6 months (range, 0.9-17.8); and the median time to complete response or better was 2.9 months (range, 0.9-17.8).[1] The longer-term data showed no new safety signals and there were no new events of cilta-cel-related neurotoxicity or movement and neurocognitive treatment emergent adverse events (TEAEs) (MNT) reported since the median ~1 year follow-up. Implementation of MNT mitigation measures has decreased the incidence rate to 0.5 percent in the CARTITUDE clinical development program.

In the 18-month follow-up data previously presented at ASCO 2021, the most common hematologic adverse events (AEs) observed were neutropenia (96 percent); anemia (81 percent); thrombocytopenia (79 percent); leukopenia (62 percent); and lymphopenia (53 percent).[2] At 18 months, 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 median time to onset of seven days (range, 1-12). Of the 92 patients with CRS, 95 percent experienced Grade 1/2 events and CRS resolved in 91 patients (99 percent) within 14 days of onset. Neurotoxicity of any grade was observed in 21 percent (n=20) of patients, with Grade 3 or higher neurotoxicity observed in 10 percent (n=10) of patients.

“Patients with heavily pre-treated multiple myeloma often have exhausted available treatment options and face poor prognoses. The updated results from the CARTITUDE-1 trial continue to suggest that cilta-cel may provide this patient population with lasting deep and durable responses,” said Thomas Martin, M.D., director of clinical research, clinical professor of medicine, Adult Leukemia and Bone Marrow Transplantation Program, interim Division Chief, co-director, Myeloma Program and co-leader, Hematopoietic Malignancies Program, at UCSF Helen Diller Family Comprehensive Cancer Center, and principal study investigator. “As a one-time infusion that shows potential to improve long-term survival and offer patients a break in ongoing treatments, cilta-cel may offer hope to patients, caregivers and physicians.”

In a subgroup analysis of CARTITUDE-1 (Abstract #3938), responses to cilta-cel were durable up to 2 years in most subgroups of patients with heavily pretreated RRMM.[3] An ORR range of 95 to 100 percent was observed in patients across all subgroups, including those with high-risk cytogenetics, International Staging System (ISS) stage III, baseline bone marrow cells ≥60 percent, and presence of baseline plasmacytomas. In patients with ISS stage III, high risk cytogenetics and with baseline plasmacytomas, median duration of response, 2-year PFS and OS appeared lower. The cilta-cel safety profile across the subgroups was consistent with the overall population, with no new safety signals.

Additionally, an adjusted indirect comparison of CARTITUDE-1 patient outcomes relative to standard-of-care therapies in real-world clinical practice (RWCP) was also featured in an oral presentation (Abstract #550).[4] The adjusted comparisons versus CARTITUDE-1 demonstrate a significantly improved ORR, complete response or better (≥CR), VGPR or better (≥VGPR), PFS and OS for the patients receiving cilta-cel compared to a diverse set of RWCP. Although patients treated with cilta-cel experienced more adverse events (AEs), including Grade 3/4 events, as compared to RWCP, overall safety profile was manageable.

CARTITUDE-2 Data Explores Use of Cilta-cel in Earlier-Line MM Settings

The Phase 2 multicohort CARTITUDE-2 study is evaluating cilta-cel safety and efficacy in various clinical settings for patients with multiple myeloma. Updated data from Cohort A of the study examined the efficacy and safety of cilta-cel in 20 patients with progressive multiple myeloma after 1-3 prior lines of therapy and who are lenalidomide-refractory (Abstract #3866).[5] At a longer median follow-up of 14.3 months, patients experienced early and deep responses with a manageable safety profile consistent with the CARTITUDE-1 study. ORR was 95 percent, which included 85 percent of patients achieving CR or better and 90 percent achieving VGPR or better. The median time to first response was one month (range, 0.7-3.3) and the median time to best response was 2.6 months (range, 0.9-7.9). The 6-month and 12-month PFS rates were 95 percent (95 percent CI, 69.5-99.3) and 84 percent (95 percent CI, 59.1-94.7), respectively. Of the 13 patients with MRD evaluable samples at the 10^{-5} cutoff threshold, 92 percent (95 percent CI, 64.0-99.8) were MRD negative.

The first data from Cohort B was also presented at ASH 2021 (Abstract #2910).[6] Cohort B included 19 patients who were in early relapse after initial therapy that included a proteasome inhibitor (PI) and immunomodulatory drug (IMiD). Data showed early and deep responses with a manageable safety profile. At a median follow-up of 10.6 months, ORR was 95 percent, which included 79 percent of patients achieving CR or better and 90 percent of patients achieving VGPR or better. The median time to first response was one month (range, 0.9-2.6) and the median time to best response was 2.5 months (range, 0.9-11.8). The 6-month and 12-month PFS rates were 90 percent (95 percent CI, 64.1-97.3) and 84 percent (95 percent CI, 57.9-94.5), respectively. Of the 13 patients with MRD evaluable samples at the 10^{-5} cutoff threshold, 92 percent (95 percent CI, 64.0-99.8) were MRD-negative.

The safety profile seen in CARTITUDE-2 Cohorts A and B were consistent with data previously reported from CARTITUDE-1. CRS occurred in 95 percent of patients in Cohort A and 84 percent of patients in Cohort B, which were mostly grades 1/2 with median time to onset of 7-8 days and median duration of ~4 days.

“The new and updated longer-term data for CARTITUDE-1 and Cohorts A and B of CARTITUDE-2 shows that responses continue to be deep and durable over time and illustrate the potential of cilta-cel to provide a new treatment option for those patients that need it the most,” said Ying Huang, PhD, CEO and CFO of Legend Biotech. “We are excited to continue to present these strong efficacy and safety results as we work toward the first regulatory approval for cilta-cel and from our robust cell therapy pipeline.”

About CARTITUDE-1

CARTITUDE-1 (NCT03548207) is a Phase 1b/2, open-label, multicenter study evaluating the safety and efficacy of cilta-cel in adults with relapsed and/or refractory with multiple myeloma who have received at least 3 prior lines of therapy or are double refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD), received a PI, an IMiD, and anti-CD38 antibody and documented disease progression within 12 months of starting the most recent therapy. The primary objective of the Phase 1b portion of the study was to characterize the safety and confirm the recommended Phase 2 dose of cilta-cel, informed by the first-in-human study with LCAR-B38M CAR-T cells (LEGEND-2). The Phase 2 portion further evaluated the efficacy of cilta-cel with overall response rate as the primary endpoint.

About CARTITUDE-2

CARTITUDE-2 (NCT04133636) is an ongoing Phase 2 multicohort study evaluating the safety and efficacy of cilta-cel in various clinical settings. Cohort A included patients who had progressive multiple myeloma after 1–3 prior lines of therapy, including PI and IMiD, were lenalidomide refractory, and had no prior exposure to BCMA-targeting agents. Cohort B included patients with early relapse after initial therapy that included a PI and IMiD. The primary objective was percentage of patients with negative minimal residual disease (MRD).

About LocoMMotion

LocoMMotion (NCT04035226) is a prospective non-interventional study evaluating the safety and efficacy of real-life standard-of-care treatments under routine clinical practice over a 24-month period in patients with RRMM. This study aims to understand the effectiveness of current standards of care in heavily pretreated patients with RRMM (reflecting real-world practice in the patient population progressing after PIs, IMiDs and anti-CD38 antibodies).

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.[7] Although treatment may result in remission, unfortunately, patients will most likely relapse.[8] 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.[9] Refractory multiple myeloma is when a patient’s disease is non-responsive or progresses within 60 days of their last therapy.[10,11] 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.[12] Patients who relapse after treatment with standard therapies, including protease inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[13]

About Cilta-cel

Cilta-cel is an investigational chimeric antigen receptor T cell (CAR-T) therapy, formerly identified as JNJ-4528 in the United States and Europe 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 United States in December 2019, cilta-cel received a Priority Medicines (PRiME) designation from the European Commission in April 2019, and a BTD in China in August 2020. In addition, Orphan Drug Designation was granted for cilta-cel by the U.S. Food and Drug Administration (FDA) in February 2019, and by the European Commission in February 2020. A Biologics License Application seeking approval of cilta-cel was submitted to the U.S. FDA and a Marketing Authorization Application was submitted to the European Medicines Agency.

About Legend Biotech

Legend Biotech is a global, clinical-stage 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 allogenic chimeric antigen receptor T-cell, T-cell receptor (TCR-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.

We are currently 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 living with multiple myeloma. Applications seeking approval of cilta-cel for the treatment of patients with RRMM are currently under regulatory review by several health authorities around the world, including the U.S. Food and Drug Administration and the European Medicines Agency.

Learn more at www.legendbiotech.com and follow us on Twitter and LinkedIn.

Cautionary Statement:

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, the anticipated timing of, and ability to progress, clinical trials, the clinical data relating to CARTITUDE-1 and CARTITUDE-2 studies and the potential benefits of our 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 or preclinical study results, including as a result of additional analysis of existing data or unexpected new 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 US litigation process; competition in general; government, industry, and general public 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 April 2, 2021. 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. 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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