Legend Biotech Announces New and Updated Data for Investigational BCMA CAR-T Ciltacabtagene Autoleucel (cilta-cel) for the Treatment of Relapsed or Refractory Multiple Myeloma at 2021 ASCO and EHA Meetings

June 1, 2021

Longer-term results from the Phase 1b/2 CARTITUDE-1 study demonstrated 98 percent overall response rate, 80 percent stringent complete response rate and 66 percent progression free survival rate at 18 months with no new safety signals

First results from the CARTITUDE-2 study of cilta-cel in earlier treatment lines will be premiered

SOMERSET, N.J.--(BUSINESS WIRE)--Jun. 1, 2021-- 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, announced today that new and updated results for ciltacabtagene autoleucel (cilta-cel), an investigational BCMA-directed CAR-T therapy for the treatment of relapsed or refractory multiple myeloma (RRMM), will be featured at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting and at the European Hematology Association (EHA) Virtual Congress.

At a median follow-up of 18 months, updated results from the Phase 1b/2 CARTITUDE-1 study including 97 heavily pretreated patients with RRMM demonstrated an overall response rate (ORR) of 98 percent, with 80 percent of patients achieving a stringent complete response (sCR), highlighting a deepening response over time (from 67 percent reported at ASH 2020).[1,2] The 18-month progression-free survival (PFS) rate was 66 percent (95 percent confidence interval [CI], 54.9-75.0) and overall survival rate (OS) rate was 81 percent (95 percent CI, 71.4-87.6). Patients had received a median of six prior lines of therapy (range, 3-18); 88 percent were triple-refractory and 42 percent were penta-refractory. Response rates were comparable (range, 95-100 percent) across prespecified subgroups, including number of prior lines of treatment, extramedullary plasmacytomas and cytogenetic risk.[1]

These data will be featured in an oral presentation at the 2021 ASCO Annual Meeting on Tuesday, June 8th (Abstract #8005) and as a poster presentation at the 2021 EHA Virtual Congress on Friday, June 11th (Abstract #EP964). The CARTITUDE-1 study supported the Biologics License Application for cilta-cel by Legend Biotech's collaborator, Janssen, which has been accepted for priority review by the U.S. Food and Drug Administration (FDA) with a Prescription Drug User Fee Act (PDUFA) target action date of November 29, 2021.

"What is remarkable about this study is that these patients, who had previously received multiple treatment regimens, have responded to cilta-cel without their disease progressing," said Saad Z. Usmani, M.D., Division Chief of Plasma Cell Disorders, Levine Cancer Institute. "These compelling results, paired with the manageable safety profile and sustained efficacy, demonstrate the potential of cilta-cel for patients with relapsed and refractory multiple myeloma."

Median time to first response was one month (range, 0.9–10.7 months) and responses deepened over time. Out of 61 minimal residual disease (MRD) evaluable patients, 92 percent achieved MRD negativity status at 10^{-5} at a median of one month (range, 0.8-7.7 months) post infusion.

Cilta-cel data showed a safety profile consistent with what has been previously reported and no new safety signals were observed with longer-term follow-up. 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). 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. There was no new incidence of neurotoxicity; 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.

"We are excited to share these latest results from the CARTITUDE-1 study which continue to show deep and sustained responses in patients who have been treated with cilta-cel," said Ying Huang, PhD, CEO and CFO of Legend Biotech. "At Legend Biotech, we are continuing our efforts to build a robust pipeline of next-generation cell therapies with the potential to address unmet needs. We look forward to our continued collaborative efforts with Janssen as we to bring this personalized treatment to patients, pending regulatory approvals."

New Data from CARTITUDE-2

For the first time, data will also be reported from Cohort A of CARTITUDE-2 (NCT04133636), a Phase 2 study evaluating the safety and efficacy of cilta-cel in patients with multiple myeloma (MM) in earlier-line settings.[3,4] Cohort A included 20 patients who had progressive MM after 1-3 prior lines of therapy and were refractory to lenalidomide, including 1 patient treated in an outpatient setting. Data showed early and deep responses with a manageable safety profile consistent with what has been observed in the CARTITUDE clinical development program. At a median follow-up of 5.8 months, ORR was 95 percent with 75 percent of patients achieving sCR or complete response. These initial results will be showcased in a poster discussion at ASCO 2021 (Abstract #8013) and as an oral presentation at the 2021 EHA Congress (Abstract #S190).

Another poster (ASCO Abstract #8028, EHA Abstract #EP1003) will discuss the incidence, mitigation and management of neurologic AEs in patients in Cohort A from the CARTITUDE-2 study.[5,6] The results show neurologic AEs were generally manageable in patients following treatment with cilta-cel. Neurotoxicities occurred in 20 percent (n=4) of patients, however, there were no movement and neurocognitive treatment-emergent AEs or Grade 3 neurotoxicity events observed in patients of Cohort A. Data from the CARTITUDE clinical development program, in which over 100 patients

have been dosed, suggest that additional patient management strategies have been successfully implemented to prevent and reduce the incidence of neurotoxicity. Cilta-cel is being investigated in patients with MM in various clinical settings as part of CARTITUDE-2 and a Phase 3 study (CARTITUDE-4, NCT04181827) in earlier settings.

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.[1,2] 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, multi-cohort, Phase 2 study evaluating the safety and efficacy of cilta-cel in with multiple myeloma. CARTITUDE-2 Cohort A includes 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. The primary objective was percentage of patients with negative minimal residual disease (MRD) status at 10^{-5}.[3,4]

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 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. 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 a 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. A Biologics License Application seeking approval of cilta-cel was accepted by the U.S. FDA and a Marketing Authorisation Application has been accepted by the European Medicines Agency.

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 best-in-class cell therapies for patients in need.

We are engaged in a strategic collaboration to develop and commercialize our lead product candidate, cilta-cel, an investigational BCMA-targeted CAR-T cell therapy for patients living 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.

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, 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 partnership with Janssen, and the data relating to CARTITUDE-1 and CARTITUDE-2 studies. 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 Annual Report filed with the Securities and Exchange Commission on April 2, 2021. 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.

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