Updated Data from LEGEND-2, a Phase 1/2 Open-label Study of BCMA-Directed CAR-T Cell Therapy LCAR-B38M Show Long-term Responses, Safety Profile, and Complete Response Rate in Treatment of Patients with Advanced Relapsed or Refractory Multiple Myeloma

Orlando, FL, December 9, 2019 – Legend Biotech reported updated data on the LEGEND-2 (NCT03090659) Phase 1/2 open-label, first-in-human study, which evaluated the investigational chimeric antigen receptor T-cell (CAR-T) therapy, LCAR-B38M, in the treatment of patients with advanced relapsed and/or refractory multiple myeloma (RRMM) in China. LCAR-B38M is a structurally differentiated CAR-T cell therapy containing a 4-1BB co-stimulatory domain and 2 BCMA-targeting single-domain antibodies designed to confer avidity. Featured in an oral presentation at the 61st American Society of Hematology (ASH) Annual Meeting (Abstract #579) and poster presentation (Abstract #1858), the study findings build upon previously reported data from the four clinical study sites: The Second Affiliated Hospital of Xi'an Jiaotong University, Shanghai Ruijin Hospital, Shanghai Changzheng Hospital, and Jiangsu Province People's Hospital. These updated results showed LCAR-B38M responses in patients who failed a median of three prior therapies. A total of 74 patients were enrolled in the LEGEND-2 study.

"The investigators are pleased to present the long-term follow-up data from the LEGEND-2 study in China for the 57 patients enrolled at the Xi'an study site," stated Baiyan Wang, MD, PhD, Department of Hematology, at the Second Affiliated Hospital of Xi'an Jiaotong University. "We are encouraged to see long-term follow-up data that further characterizes LCAR-B38M's potential to provide a meaningful therapeutic option that may achieve and maintain deep and durable responses with a generally well-tolerated safety profile."

In the study update (data cut-off July 31, 2019) presented by Baiyan Wang, MD, PhD, 57 patients with RRMM received LCAR-B38M CAR-T cell therapy (median administered dose 0.5×10^6 cells/kg; range, $0.07–2.1\times10^6$ CAR+ T cells/kg) at The Second Affiliated Hospital of Xi'an Jiaotong University clinical study site. The median age of the patients was 54 years (range, 27–72 years). The median number of prior therapies was 3 (range, 1–9). Seventy-four percent of patients had stage 3 disease by Durie-Salmon staging and 37% of patients had stage 3 disease by ISS staging.

According to study findings, there was an 88% overall response rate (ORR). Complete response (CR) was achieved by 74% of patients; very good partial response (VGPR) was achieved by 4% of patients; and partial response was achieved by 11% of patients. With a median follow-up of 25 months, the median duration of response (DOR) was 27 months (95% CI, 14.3-not evaluable [NE]) for all patients. A median progression-free survival (PFS) of 19.9 months (95% CI, 9.6–31.0) and the median overall survival (OS) of 36.1 months (95% CI, 26.4–NE) was observed for all patients.

The most common adverse events (AEs) were pyrexia (91%), cytokine release syndrome (CRS) (90%), thrombocytopenia (49%), and leukopenia (47%). In patients who experienced grade 3/4 AEs (65%), the most common were leukopenia (30%), thrombocytopenia (23%), and increased aspartate aminotransferase (21%). CRS was mostly low grade, which included grade 1 (47%), grade 2 (35%), and grade 3 (7%). The median time to onset of CRS was 9 days (range, 1-19 days), with a median duration of 9 days (range, 3-57 days). Neurotoxicity was observed in one patient who had grade 1 aphasia, agitation, and seizure-like activity.

Additionally, Lijuan Chen, MD, PhD, Ruijin Hospital affiliated with Shanghai Jiao Tong University School of Medicine, presented a study update (data cut-off October 31, 2019) for 17 patients with RRMM who were enrolled at the Shanghai Ruijin Hospital, Shanghai Changzheng Hospital, and Jiangsu Province People's Hospital and received LCAR-B38M CAR-T cell therapy (mean administered dose $0.7x10^6$; range, $0.2–1.5x10^6$ CAR+ T cells/kg). The median age of the patients was 56 years (range, 35-73 years). The median number of prior therapies was 4 (range, 3-11). According to study findings, there was an 88% ORR. CR was achieved by 82% percent of patients and VGPR was achieved by 6% of patients. The median time to first response was approximately 1 month. With a median follow-up of 26 months (0.4–30), a median PFS of 18 months (95% CI: 9–NE) was observed for all patients. The median OS has not been reached (95% CI: 12–NE).

The most common AEs were CRS (100%), cytopenia (82%), and increased aspartate aminotransferase (94%). There was one grade 5 AE of CRS using CAR-T cell therapy-associated toxicity (CARTOX) criteria.

"We are encouraged to see the long-term follow-up data for the LEGEND-2 study in China," stated Yuan Xu, PhD, CEO of Legend Biotech. "As the results for the CARTITUDE-1 study in the United States emerge, we observe the initial safety and efficacy data are consistent with the LEGEND-2 study. In collaboration with Janssen, Legend Biotech is dedicated to advancing the clinical development program of LCAR-B38M/JNJ-4528* for patients with RRMM."

Initial results from the CARTITUDE-1 (NCT03548207) study premiered at ASH 2019 as an oral presentation and highlighted in the official ASH press program (Abstract #577).

**LCAR-B38M identifies the investigational product being studied in China, and JNJ-68284528 (JNJ-4528) identifies the investigational product being studied in the United States/European Union, both of which are representative of the same CAR-T cell therapy. In December 2017, Legend Biotech, USA Inc, and Legend Biotech Ireland Limited ("Legend"), subsidiaries of GenScript Biotech Corporation entered into a worldwide collaboration and license agreement with Janssen Biotech, Inc. (Janssen), to jointly develop and commercialize LCAR-B38M in multiple myeloma. Globally, Legend, together with Janssen, is advancing JNJ-4528 in a comprehensive clinical development program to evaluate its efficacy and safety in adults with advanced RRMM.*

About the Clinical Development Program

CARTITUDE-1

In the US, JNJ-4528 is currently being investigated in the Phase 1b/2 CARTITUDE-1 (MMY2001, NCT03548207)[1] registration study for the treatment of patients with multiple myeloma who have received at least 3 prior lines of therapy or are double refractory to a PI and IMiD®; received a PI, an IMiD; and anti-CD38 antibody; and documented disease progression within 12 months of starting the most recent therapy.

CARTITUDE-2

In the global, multi-cohort Phase 2 CARTITUDE-2 (MMY2003, NCT04133636)[2] study, JNJ-4528 will be investigated in patients with multiple myeloma in various clinical settings. This study is being conducted to evaluate the overall minimal residual disease (MRD) negative rate of participants who receive JNJ-4528.

CARTITUDE-4

In the global, Phase 3 CARTITUDE-4 (MMY3002, NCT04181827)[3)] study, JNJ-4528 will be investigated in patients with multiple myeloma who have received 1-3 prior lines of therapy including a PI and IMiD and are refractory to lenalidomide. The study is being conducted to evaluate the efficacy of JNJ-4528 compared to standard therapies[4] including daratumumab, pomalidomide and low-dose dexamethasone (DPd) or pomalidomide, bortezomib and

low-dose dexamethasone (PVd).

LEGEND-2 and CARTIFAN-1

LEGEND-2 (NCT03090659)[5] is an ongoing single-arm, open-label Phase 1/2 study of 74 patients being conducted at four participating hospitals in China evaluating the efficacy and safety of LCAR-B38M for the treatment of relapsed or refractory multiple myeloma.

The Phase 2 CARTIFAN-1 confirmatory trial (MMY2002, NCT03758417)[6] registered with the China Center for Drug Evaluation (CTR20181007), is actively recruiting to further evaluate LCAR-B38M in patients with advanced RRMM.

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.[7,8]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[9] Refractory multiple myeloma is when a patient's disease is non-responsive or progresses within 60 days of their last therapy.[10,11] 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.[12] 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.[13] Patients who relapse after treatment with standard therapies, including protease inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[14] In 2019, the American Cancer Society projects that 32,110 new cases of multiple myeloma and 12,960 deaths will occur in the US.[15]

About Legend Biotech

Legend Biotech is a clinical stage biopharmaceutical company engaged in the discovery and development of novel cell therapies in hematology/oncology, infectious diseases and auto-immune disorders. Legend is a subsidiary of GenScript Biotech Corporation (HKEx: 1548), which operates in the USA, Hong Kong, mainland China and Ireland. Learn more at www.LegendBiotech.com.

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