Initial Data from Phase 1b/2 Study of BCMA-Directed CAR-T Cell Therapy JNJ-4528 Show Early and High Responses in Advanced Relapsed or Refractory Multiple Myeloma

Orlando, FL, December 7, 2019 – Legend Biotech announced today initial results from the Janssen Research & Development, LLC (Janssen)-sponsored Phase 1b/2 CARTITUDE-1 study (NCT03548207) evaluating the efficacy and safety of JNJ-68284528 (JNJ-4528), an investigational B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T cell (CAR-T) therapy being evaluated in the treatment of patients with relapsed and/or refractory multiple myeloma (RRMM). JNJ-4528 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[1]. The study enrolled patients who have received at least three prior lines of therapy or are double refractory to a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD®); have received a PI, IMiD and an anti-CD38 antibody; and who progressed on or within 12 months of their last line of therapy. The initial CARTITUDE-1 study results were reported at the American Society of Hematology (ASH) Annual Meeting and highlighted in the official ASH press program (Abstract #577).

"We are pleased to share the initial data from the CARTITUDE-1 study in the United States which build upon the first-in-human LEGEND-2 study conducted in China," said Deepu Madduri, M.D., Assistant Professor of Medicine, Hematology and Medical Oncology, Tisch Cancer Institute at Mount Sinai, New York, and principal study investigator.

With a data cut-off date of November 6, 2019 (N=29), the median age of the patients was 60 years (range, 50 –75 years), the median number of prior therapies was 5 (range, 3–18), and the median administered dose of JNJ-4528 was $0.73x10^6$ CAR+ viable T cells/kg. All patients were triple-exposed and 25 patients (86%) were triple-refractory to a proteasome inhibitor (PI), immunomodulatory drug (IMiD®) and anti-CD38. Twenty-one patients (72%) were penta-exposed and 9 patients (31%) were penta-refractory to ≥2 PIs, ≥2 IMiDs, and anti-CD38.

According to study findings, there was a 100% overall response rate (ORR) (95 percent confidence interval [CI], 76-95). Complete response (CR) or better (≥CR) was achieved by 69% of patients (95 percent CI, 60-85); very good partial response (VGPR) or better (≥ VGPR) was achieved by 86% of patients; and partial response was achieved

by 14% of patients. Moreover, 66% of patients had a stringent CR, meaning that sensitive laboratory and microscopic tests found no evidence for myeloma proteins or cells in blood, urine and bone marrow.

Notably, 100% of evaluable patients who achieved ≥CR were minimal residual disease (MRD)-negative at 10^{-5} sensitivity threshold. With a median follow-up of 6 months, 27 of 29 patients remained progression-free.

The most common adverse events (AEs) were cytokine release syndrome (CRS) (93%), neutropenia (93%), thrombocytopenia (86%), and anemia (86%). CRS was reported in 27 patients (93%) and was mostly grade 1 – 2. The majority of patients (80%) had grade 1–2 CRS, with 1 grade 3 event and 1 grade 5 event at day 99 from sequalae of grade 4 CRS (dose-limiting toxicity). In patients with CRS, median time of onset was 7 days, with >90% between days 5 – 9. Neurotoxicity (ICANS) was infrequently observed in the context of CRS and generally low-grade (1 patient with grade 3).

Additionally, data highlighting post-infusion CAR+ T cell expansion in the bone marrow and blood of patients enrolled in the CARTITUDE-1 study will be reported (Abstract #928) during an oral presentation at ASH. While both CD4+ and CD8+ CAR+ T cells expanded in vivo, a preferential expansion of memory CD8+ CAR+ T cells was observed at peak expansion. These and other correlative studies are being conducted to better understand the immune mechanisms associated with response to JNJ-4528, and suggest that the high anti-myeloma activity of JNJ-4528 seen at a relatively low T cell dose is potentially related to its preferential and consistent in vivo expansion of CD8+ CAR+ T cells.

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

Long-term follow-up data for the Phase 1/2 LEGEND-2 study in China are reported during an oral presentation (Abstract #579) and poster presentation (Abstract #1858) at ASH.

**LCAR-B38M identifies the investigational product being studied in China, and JNJ-68284528 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)[2] 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)[3] 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)[4] 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[5] including daratumumab, pomalidomide and low-dose dexamethasone (DPd) or pomalidomide, bortezomib and low-dose dexamethasone (PVd).

LEGEND-2 and CARTIFAN-1

LEGEND-2 (NCT03090659)[6] 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)[7] 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.[8,9]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[10] Refractory multiple myeloma is when a patient's disease is non-responsive or progresses within 60 days of their last therapy.[11, 12] 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.[13] 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.[14] Patients who relapse after treatment with standard therapies, including protease inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[15] In 2019, the American Cancer Society projects that 32,110 new cases of multiple myeloma and 12,960 deaths will occur in the US.[16]

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.

Cautions Concerning Forward-Looking Statements

This information constitutes forward-looking statements relating to the business of Legend Biotech, including express or implied discussions regarding the clinical development of its product candidates and potential attributes and benefits of such product candidates. Such forward-looking statements reflect the current views of Legend's management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. In particular, Legend's expectations could be affected by, among other things, uncertainties involved in the development of new pharmaceutical products; unexpected clinical trial results, including additional analysis of existing clinical data or unexpected new clinical data; unexpected regulatory actions or delays or government regulation generally; Legend's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing and other political pressures. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

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.

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