Updated Results from Phase 1b/2 Study of BCMA CAR-T Therapy JNJ-4528 Shows Early, Deep and Durable Responses in Heavily Pretreated Patients with Relapsed or Refractory Multiple Myeloma

Longer-term follow up data (median of 11.5 months) from the Phase 1b portion of the CARTITUDE-1 study demonstrated 100% overall response rate, 86% stringent complete response rate and a 9 month progression free survival rate of 86%.

Somerset, N.J., May 13, 2020 – Legend Biotech Corporation ("Legend") announced today updated results from the Janssen Pharmaceutical Companies of Johnson & Johnson ("Janssen") sponsored Phase 1b/2 CARTITUDE-1 study (NCT03548207)[1] 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 in the treatment of patients with relapsed or refractory multiple myeloma. JNJ-4528 is a structurally differentiated CAR-T cell therapy containing a 4-1BB co-stimulatory domain and two BCMA-targeting single-domain antibodies designed to confer avidity.[2]

Longer-term follow-up results from the Phase 1b portion of the study (n=29), to be shared in an oral presentation at the American Society of Clinical Oncology (ASCO) Virtual Scientific Program (Abstract #8505), show that all patients responded to treatment and that the responses were deep and durable with 86 percent of patients achieving stringent complete response at a median follow-up time of 11.5 months. In addition, results showed a 100 percent overall response rate (ORR), which included 97 percent of patients achieving a very good partial response or better and three percent achieving a partial response. The median time to first response was one month (range, 1-3), and 81 percent of evaluable patients (n=16) achieved minimal residual disease (MRD)-negative disease status at 10^{-5} or 10^{-6} at the time of first suspected complete response. The 9-month progression free survival rate was 86 percent and 22 of 29 patients remained alive and progression free at the time of data cut-off. Patients in the study were heavily pre-treated and received a median dose of 0.72×10^6 CAR+ viable T cells/kg.[3]

Patients evaluated received a median of five (range, 3-18) prior treatment regimens; 86 percent were triple-refractory and 28 percent were penta-refractory.

"The longer-term results for JNJ-4528, as demonstrated through the latest findings from the CARTITUDE-1 study, show the continued treatment effect for heavily pre-treated patients who faced a poor prognosis," said Jesus G. Berdeja, M.D., Director of Myeloma Research, Sarah Cannon Research Institute, and principal study investigator. "We're encouraged by not only the relatively high rate of stringent complete responses, but the strong progression-free survival results seen in these patients."

The most common adverse events (AEs) observed in CARTITUDE-1 were neutropenia (100 percent) and cytokine release syndrome (CRS) (93 percent). The median time to onset of CRS was seven days (range, 2-12) post-infusion, with a majority of patients experiencing Grade 1-2 CRS and two patients experiencing Grade 3 or greater CRS. In patients who experienced Grade 3 and above AEs, the most common were neutropenia (100 percent), thrombocytopenia (69 percent), and leukopenia (66 percent). Neurotoxicity consistent with ICANS was observed in 3 patients (10 percent) including 1 patient (3 percent) with ≥ Grade 3 toxicity. There were 3 deaths during the Phase 1b

study: one due to CRS, one due to acute myeloid leukemia (not treatment-related), and one due to progressive disease.[3]

"We are heartened by the follow-up data from the Phase 1b portion of the CARTITUDE-1 study as they further support the findings from the LEGEND-2 study in China, with both demonstrating deep, durable treatment responses," said Yuan Xu, PhD, Chief Executive Officer and Board Member of Legend Biotech. "We remain committed to work closely with our strategic partner and key stakeholders to advance JNJ-4528 through clinical development, in line with our mission to deliver innovative cell therapy options to patients living with cancer."

About CARTITUDE-1

CARTITUDE-1 (NCT03548207) is an ongoing Phase 1b/2, open-label, multicenter study evaluating the safety and efficacy of JNJ-4528 in adults with relapsed or refractory multiple myeloma. Of the patients in the Phase 1b portion (n=29), 97 percent were refractory to last line of treatment and 86 percent were triple-class refractory, meaning their cancer did not respond to an immunomodulatory agent (IMiD), a proteasome inhibitor (PI) and an anti-CD38 antibody.

The primary objective of the Phase 1b portion of the study was to characterize the safety and confirm the dose of JNJ-4528, informed by the first-in-human study with LCAR-B38M CAR-T cells (LEGEND-2). Based on the safety profile observed in this portion of the study, outpatient dosing will be evaluated in additional CARTITUDE studies. The Phase 2 portion of the study will evaluate the efficacy of JNJ-4528 with overall response as the primary endpoint.

About JNJ-4528 (LCAR-B38M)

JNJ-4528 (LCAR-B38M) is an investigational CAR-T therapy for the treatment of patients with RRMM. The design comprises a structurally differentiated CAR-T with two BCMA-targeting single domain antibodies.

JNJ-4528 identifies the investigational product being studied in the US, Europe, and Japan. LCAR-B38M identifies the investigational product being studied in China. Both represent the same CAR-T cell therapy.

In December 2017, Legend Biotech, USA Inc., and Legend Biotech Ireland Limited, entered into a worldwide collaboration and license agreement with Janssen, to jointly develop and commercialize JNJ-4528/LCAR-B38M in multiple myeloma.

In May 2018[4], Legend announced that the U.S. Food and Drug Administration (FDA) authorized Janssen to initiate a Phase 1b/2 trial (NCT03548207)[1] to evaluate the efficacy and safety of JNJ-4528 in adults with RRMM, informed by the LEGEND-2 (NCT03090659)[5] study results.

In December 2019[6], Legend announced that the FDA granted Janssen Breakthrough Therapy Designation, which is granted to expedite the development and regulatory review of an investigational medicine that is intended to treat a serious or life-threatening condition.[7] In February 2019[8], the U.S. FDA granted Janssen an Orphan Drug Designation for JNJ-4528. In April 2019[9], JNJ-4528 was granted PRIME (PRIority MEdicines) designation by the European Medicines Agency (EMA). PRIME offers enhanced interaction and early dialogue to optimize development plans and speed up evaluation of cutting-edge, scientific advances that target a high unmet medical need.[10] In February 2020, the European Commission granted Janssen an Orphan Drug Designation for JNJ-4528.[11]

About Multiple Myeloma

Multiple myeloma is currently an incurable blood cancer that starts in the bone marrow and is characterized by an excessive proliferation of plasma cells.[12] Although treatment may result in remission, patients will most likely relapse as there is currently no cure.[13] Refractory multiple myeloma is when a patient's disease is nonresponsive or progresses within 60 days of their last therapy.[14,15] 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.[16] 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.[17] Patients who relapse after treatment with standard therapies, including protease inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[18]

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. Legend Biotech has functional sites in the United States, Europe, and mainland China. Learn more at https://www.legendbiotech.com/.

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