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News Release

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Early, Deep, Durable Responses of Ciltacabtagene Autoleucel (cilta-cel) Observed in Phase 1b/2 CARTITUDE-1 Study Show Potential of BCMA CAR-T in Treatment of Heavily Pretreated Patients with Multiple Myeloma

Combined results from Phase 1b/2 CARTITUDE-1 study presented at ASH 2020 show 97 percent overall response rate at median follow-up of 12.4 months[1]

BEERSE, BELGIUM, 05 December 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today longer-term results from the combined Phase 1b/2 CARTITUDE-1 study (NCT03548207) evaluating the efficacy and safety of ciltacabtagene autoleucel (cilta-cel), an investigational B cell maturation antigen (BCMA)-directed chimeric antigen receptor T cell (CAR-T) therapy, for the treatment of patients with relapsed and/or refractory multiple myeloma. These data, presented as an oral presentation at the American Society of Hematology (ASH) 2020 Annual Meeting (Abstract #177), continued to demonstrate a very high overall response rate of 97 percent, which deepened over time with 67 percent of patients achieving a stringent complete response.[1] With a median follow-up of 12.4 months, median duration of response and progression-free survival (PFS) were not reached.[1]

"Unfortunately, for patients with multiple myeloma for whom at least three established treatment regimens have stopped working, the prognosis is often not good," said Deepu Madduri,* M.D., Assistant Professor of Medicine, Hematology and Medical Oncology, The Tisch Cancer Institute at Mount Sinai, New York, and principal study investigator. "In the CARTITUDE-1 study, heavily pretreated patients, including those who were triple-class refractory, achieved an impressive response following a single infusion of ciltacabtagene autoleucel."

Median time to first response was one month (range, 0.9-8.5), with responses observed at a low dose of CAR-T cells (median administered dose $0.71x10^6$ CAR+ viable T cells/kg) and were ongoing in 72 percent (n=70) of patients. Additionally, 93 percent of evaluable patients (n=53) achieved minimal residual disease (MRD) negative disease status at 10^{-5}.[1] The trial included heavily pretreated patients, with evaluated patients having received a median of six prior treatment regimens (range, 3-18); 88 percent (n=85) were triple-refractory, 42 percent (n=41) were penta-refractory, and 99 percent (n=96) were refractory to the last line of therapy.[1] The 12-month PFS rate was 77 percent (95 percent confidence interval [CI], 66-84).[1] The 12-month overall survival (OS) rate was 89 percent (95 percent CI, 80-94) and manufacturing of cilta-cel was successful for all patients.[1]

"The combined Phase 1b/2 data from the CARTITUDE-1 study include a larger patient population than previously reported in the initial Phase 1b results, and we are encouraged that patients treated with cilta-cel continued to achieve impressive, deep responses," said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Research Development, Janssen Research & Development, LLC. "The responses also appeared to be durable as indicated by the estimate that 89 percent of patients remained alive and 77 percent of patients remained progression-free after one year of follow up."

"We are committed to applying the best science and disease insights to bring transformational therapies for people living with blood cancers," adds Dr Catherine Taylor, Vice President, Medical Affairs Therapeutic Area Strategy, Europe, Middle East and Africa (EMEA), Janssen-Cilag Ltd., Middle East. "We are excited to see these latest results reinforce the early promising data previously

presented and hope that one day cilta-cel can offer a viable treatment option for multiple myeloma patients who have limited therapeutic options."

In these combined results, the most common haematologic 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).[1] 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 99 percent of which were resolved within 14 days of onset.[1] Of the 92 patients with CRS, 95 percent (n=87) were Grade 1/2, three percent (n=3) were Grade 3, one percent (n=1) was Grade 4 and one percent (n=1) was Grade 5.[1] The median onset of CRS was at seven days (range, 1-12) post-infusion, with 89 percent (n=82) of patients experiencing CRS onset at day four or later.[1]

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.[1] Of these, Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS) was observed in 16 patients; other neurotoxicities were observed in 12 patients and generally occurred after resolution of CRS and/or ICANS.[1] ICANS events were resolved in all patients with a median time to recovery of four days (range, 1-12).[1] Other neurotoxicities were resolved in six patients with a median time of 75 days (range, 2-160) and were not resolved in six patients (one with ongoing toxicity, one died from neurotoxicity and four died due to other causes).[1] Fourteen deaths were reported during the study: five due to disease progression, three due to adverse events unrelated to treatment (acute myelogenous leukemia (n=2), pneumonia (n=1)) and six due to adverse events related to treatment (sepsis and/or septic shock (n=2), CRS/ hemophagocytic lymphohistiocytosis (n=1), lung abscess (n=1), respiratory failure (n=1) and neurotoxicity (n=1)).[1]

**Deepu Madduri is the lead investigator of the CARTITUDE-1 study. She was compensated for media work during the American Society of Hematology (ASH) 2020 Annual Meeting*

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About CARTITUDE-1

CARTITUDE-1 (NCT03548207) is an ongoing Phase 1b/2, open-label, multicentre study evaluating the safety and efficacy of cilta-cel in adults with relapsed and/or refractory multiple myeloma, 99 percent of whom were refractory to the last line of treatment; 88 percent of whom were triple-class refractory, meaning their cancer did not, or no longer responds to an immunomodulatory agent (IMiD), a proteasome inhibitor (PI) and an anti-CD38 antibody.[1,2]

The primary objective of the Phase 1b portion of the study, involving 29 patients, was to characterise the safety and confirm the dose of cilta-cel, informed by the first-in-human study with LCAR-B38M CAR-T cells (LEGEND-2).[2] Based on the safety profile observed in this portion of the study.[1] The Phase 2 portion of the study, is evaluating the efficacy of cilta-cel with overall response as the primary endpoint.[1]

About Ciltacabtagene Autoleucel (cilta-cel)

Cilta-cel is an investigational chimeric antigen receptor T cell (CAR-T) therapy for the treatment of patients with multiple myeloma. The design comprises a structurally differentiated CAR-T with two BCMA-targeting single domain antibodies.[1] CAR-T cells are an innovative approach to eradicating cancer cells by harnessing the power of a patient's own immune system.[3] BCMA is a protein that is highly expressed on myeloma cells.[4]

In December 2017, Janssen entered into an exclusive worldwide license and collaboration agreement with Legend Biotech to develop and commercialise cilta-cel.[5] In May 2018, Janssen initiated a Phase 1b/2 CARTITUDE-1 trial (NCT03548207) to evaluate the efficacy and safety of cilta-cel in adults with relapsed and/or refractory multiple myeloma, informed by the LEGEND-2 study results.[2]

In April 2019, cilta-cel was granted PRIME (PRIority MEdicines) designation by the European Medicines Agency (EMA).[6] PRIME offers enhanced interaction and early dialogue to optimise drug development plans and speed up evaluation of cutting-edge, scientific advances that target a high unmet medical need.[7] In

February 2020, the European Commission granted orphan designation for cilta-cel.[8]

About Multiple Myeloma

Multiple myeloma (MM) is an incurable blood cancer that starts in the bone marrow and is characterised by an excessive proliferation of plasma cells.[9] In Europe, more than 48,200 people were diagnosed with MM in 2018, and more than 30,800 patients died.[10] Around 50 percent of newly diagnosed patients do not reach five-year survival,[11,12] and almost 29 percent of patients with multiple myeloma will die within one year of diagnosis.[13]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[14] Refractory MM is when a patient's disease progresses within 60 days of their last therapy.[15] Relapsed cancer is when the disease has returned after a period of initial, partial or complete remission.[15] While some patients with MM have no symptoms at all, others are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[16] Patients who relapse after treatment with standard therapies, including protease inhibitors and immunomodulatory agents, have poor prognoses and require new therapies for continued disease control.[17]

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension. Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen-Cilag Ltd., Middle East and Janssen Research and Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of ciltacabtagene autoleucel. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV and/or any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 29, 2019, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. Neither the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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