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New Data from CARTITUDE-1 Study Show Continued Deep and Durable Responses of Ciltacabtagene Autoleucel (cilta-cel) in Treatment of Heavily Pre-treated Patients with Multiple Myeloma

Data presented at ASH 2021 congress show 83 percent of patients achieved a stringent complete response at median follow-up of 22 months[1]

92 percent of evaluable patients achieved minimal residual disease negativity (10^{-5}), with progression-free survival and overall survival sustained in those patients for ≥six and ≥12 months[1]

BEERSE, BELGIUM, 12 December 2021– The Janssen Pharmaceutical Companies of Johnson & Johnson announced today longer-term results from the Phase 1b/2 CARTITUDE-1 study 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 administered as a single infusion, in the treatment of patients with relapsed and/or refractory multiple myeloma.[1] The data, featured as an oral presentation at the American Society of Hematology (ASH) 2021 Annual Meeting (Abstract #549) and selected as part of the Highlights of ASH programme, show that patients receiving cilta-cel demonstrate deep and durable responses, with a very high overall response rate (ORR) of 98 percent.[1]

Responses in the 97 patients treated with cilta-cel deepened over time, with 83 percent of patients achieving a stringent complete response (sCR) at median 22-month follow-up, an increase from 80 percent at the 18-month median follow-up data presented at the 2021 American Society of Clinical

Oncology (ASCO) Annual Meeting, and from 67 percent at the 12.4-month median follow-up data presented at ASH 2020.[1,2,3] At median follow-up of 22 months, median progression-free survival (PFS) and median overall survival (OS) were not reached, suggesting long-term durability of responses and survival for patients.[1] Two-year PFS and OS rates were 61 percent (95 percent Confidence Interval [CI], 48.5–70.4) and 74 percent (95 percent CI, 61.9–82.7), respectively.[1] Among 61 minimal residual disease (MRD) evaluable patients, 92 percent of patients achieved MRD negativity (at 10^{-5}).[1] The two-year PFS rates in patients who achieved MRD negativity for ≥six and ≥12 months were 91 percent (95 percent CI, 67.1–97.8) and 100 percent, respectively.[1]

"Unfortunately, patients with multiple myeloma for whom at least three treatment regimens have stopped working, face a median survival of less than a year with currently available treatments," said Thomas Martin, M.D.,* Director of Clinical Research, Clinical Professor of Medicine, Adult Leukemia and Bone Marrow Transplantation Program, Associate Director, Myeloma Program and Co-Leader, Hematopoietic Malignancies Program, at UCSF Helen Diller Family Comprehensive Cancer Center, and principal study investigator. "The CARTITUDE-1 data presented at ASH 2021 builds upon previous results that show that a single infusion of cilta-cel resulted in durable responses and survival across the study population, further supporting the potential of cilta-cel in offering patients and physicians a valuable new treatment option."

Median time to first response was one month (range, 0.9–10.7), with responses deepening over time.[1] Additionally, median time to best response was 2.6 months (range, 0.9–17.8) and median time to complete response or better was 2.9 months (range, 0.9–17.8).[1] Twelve percent of patients achieved a very good partial response and three percent achieved a partial response.[1] The study included patients who received a median of six prior treatment regimens (range, 3–18).[1] All patients were triple-class [immunomodulatory agent (IMiD), proteasome inhibitor (PI) and an anti-CD38 antibody] exposed, while 42 percent of patients were penta-drug refractory and 99 percent of patients were refractory to the last line of therapy.[1]

"These data add to the growing body of evidence supporting the potential clinical benefit of cilta-cel in the treatment of patients with relapsed and/or refractory multiple myeloma, a population in need of new options," said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Research and Development, Janssen Research & Development, LLC. "We look forward to further evaluation of cilta-cel as part of our comprehensive CARTITUDE clinical development programme that includes studying cilta-cel in patients with newly diagnosed multiple myeloma."

The data demonstrated a consistent safety profile for cilta-cel and no new safety signals were observed with longer follow-up.[1] In 18-month follow-up data presented at ASCO 2021, the most common haematologic adverse events (AEs) observed were neutropenia (96 percent); anaemia (81 percent); thrombocytopenia (79 percent); leukopenia (62 percent); and lymphopenia (53 percent).[2] At 18 months, 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 resolved within 14 days of onset.[2] Of the 92 patients with CRS at 18-month follow-up, 95 percent experienced grade 1/2 events.[2] Neurotoxicity of any grade was observed in 21 percent (n=20) of patients at 18 months, with grade 3 or higher neurotoxicity observed in 10 percent (n=10) of patients.[2] There were no new events of cilta-cel–related neurotoxicity or movement and neurocognitive treatment (MNT) emergent adverse events reported in CARTITUDE-1 since the median 12.4-month follow-up data were presented at ASH 2020.[1,3] At the 22-month data cut-off, more than 200 patients have been dosed with cilta-cel across the CARTITUDE clinical development programme and MNT incidence has decreased to less than one percent since the implementation of MNT mitigation measures.[1]

"We are pleased that we are again able to present longer-term follow-up data, this time at nearly two years, for this innovative potential treatment for people living with relapsed/refractory multiple myeloma." said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "The sustained efficacy and consistent safety profile build on the strong results seen to date and may bring us one step closer to changing the expectations of what a multiple myeloma diagnosis means for patients."

Subgroup Analysis of the Phase 1b/2 CARTITUDE-1 Study

In the abstract accepted for presentation at ASH 2021, data demonstrated that cilta-cel resulted in deep, durable responses in all evaluated subgroups in CARTITUDE-1 at median follow-up of 18 months.[4] An ORR range of 95 to 100 percent was observed in patients across all subgroups, including those with high-risk cytogenetics, International Staging System (ISS) stage III multiple myeloma, baseline bone marrow cells ≥60 percent, and presence of baseline plasmacytomas.[4] In patients with ISS stage III, high risk cytogenetics and with baseline plasmacytomas, median duration of response appeared shorter and 18-month PFS and OS rates lower.[4] The cilta-cel safety profile across the subgroups was consistent with the overall population, with no new safety signals.[4] The latest data from this analysis will be presented in a poster presentation (Abstract #3938) at ASH 2021 on Monday, December 13.[4]

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About CARTITUDE-1

CARTITUDE-1 (NCT03548207)[5] 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 respond, or no longer responds, to an immunomodulatory agent (IMiD), a proteasome inhibitor (PI) and an anti-CD38 antibody.[1]

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).[1,5,6] Based on the safety profile observed in this portion of the study, outpatient dosing is being evaluated in additional CARTITUDE studies. The Phase 2 portion of the study, involving 68 additional patients, is evaluating the efficacy of cilta-cel with overall response as the primary endpoint.[1,5]

About Ciltacabtagene Autoleucel (cilta-cel)

Cilta-cel is an investigational chimeric antigen receptor T-cell (CAR-T) therapy that is being studied in a comprehensive clinical development programme for the treatment of patients with relapsed or refractory multiple myeloma and in earlier lines of treatment.[1] The design consists of a structurally differentiated CAR-T with two BCMA-targeting single domain antibodies.[1] In December 2017, Janssen Biotech, Inc. (Janssen) entered into an exclusive worldwide license and collaboration agreement with Legend Biotech to develop and commercialise cilta-cel.[7]

In April 2021, Janssen announced its submission of a Marketing Authorisation Application (MAA) to the European Medicines Agency seeking approval of cilta-cel for the treatment of patients with relapsed and/or refractory multiple myeloma.[8] In December 2020, Janssen announced initiation of a rolling submission of its Biologics License Application (BLA) to the United States (U.S.) Food and Drug Administration (FDA) for cilta-cel.[9] In addition to U.S. Breakthrough Therapy Designation in December 2019, cilta-cel received a PRIority MEdicines (PRiME) designation from the European Commission in April 2019, and a Breakthrough Therapy Designation in China in August 2020.[10,11] Janssen also received Orphan Drug Designation for cilta-cel from the European Commission in February 2020.[12]

About Multiple Myeloma

Multiple myeloma is currently an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[13] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow.[13] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,500 patients died.[14] While some patients with multiple myeloma have no symptoms, most patients are diagnosed due to symptoms, which can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, kidney problems or infections.[15]

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 Pharmaceutical NV, Janssen Research & Development, LLC, and Janssen-Cilag Limited are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

**Thomas Martin, M.D. has been a paid consultant to Janssen; he has not been paid for any media work.*

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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 ciltacabtagene autoleucel (cilta-cel). 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 Pharmaceutical NV, 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 behaviour 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 January 3, 2021, 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. None of 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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