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News Release

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Longer-term Data from CARTITUDE-1 Study Demonstrate Continued Deep and Durable Responses to CARVYKTI® (ciltacabtagene autoleucel) in Heavily Pretreated Patients with Relapsed or Refractory Multiple Myeloma

At nearly 28 months of median follow-up, median progression-free survival and overall survival were not yet reached[1]

Data presented at the 2022 ASCO Annual Meeting and published in the Journal of Clinical Oncology

BEERSE, BELGIUM, 4 June 2022– The Janssen Pharmaceutical Companies of Johnson & Johnson announced today updated results from the Phase 1b/2 CARTITUDE-1 study evaluating the efficacy and safety of CARVYKTI® (ciltacabtagene autoleucel; cilta-cel), a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T-cell (CAR-T) therapy. The study included patients with relapsed or refractory multiple myeloma who had received ≥3 lines of therapy, which included an immunomodulatory agent (IMiD), proteasome inhibitor (PI) and an anti-CD38 monoclonal antibody or were double refractory to an IMiD and PI and who had received a PI, an IMiD and an anti-CD38 as part of previous therapy. These data, featured as a poster presentation at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #8028), were simultaneously published in the *Journal of Clinical Oncology*.[2]

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Triple-class exposed patients often experience poorer outcomes, with a recent study indicating a median overall survival (OS) of 9.3 months.[3] The new CARTITUDE-1 results showed that at a median follow-up of nearly 28 months (27.7), in 97 patients treated with cilta-cel, the overall response rate (ORR) remained consistent at 98 percent (95 percent Confidence Interval [CI], 92.7–99.7), with 83 percent (95 percent CI, 73.4–89.4) of patients treated with cilta-cel achieving a stringent complete response (sCR).[1] The responses were durable, and median OS and progression free survival (PFS) were not reached. PFS and OS rates at 28 months follow-up were 55 percent (95 percent CI, 44.0 to 64.6) and 70 percent (95 percent CI, 60.1 to 78.6), respectively.[1]

Sixty-one patients had samples evaluable for minimal residual disease status (MRD), 92 percent of whom achieved MRD negativity at the 10^{-5} threshold, which was sustained for ≥6 months in 68 percent (34/50 with sufficient follow-up) and ≥12 months in 55 percent (24/44 with sufficient follow-up).[1] In those same patients, two-year PFS rates were 73 percent (95 percent CI, 52.1 to 85.9) and 79 percent (95 percent CI, 51.5 to 91.8), respectively, and two-year OS rates were 94 percent (95 percent CI, 76.1 to 98.3) and 91 percent (95 percent CI, 67.7 to 97.6), respectively.[1] Both the two-year PFS and OS rates were favourable compared to the overall study population.[1]

"These latest results further reinforce the value of cilta-cel as a welcome new addition to the way in which we treat, and ultimately extend, remission for triple-exposed patients, where the need for innovation remains high," said Maria-Victoria Mateos, M.D., Ph.D., Consultant Physician in Haematology, University Hospital of Salamanca.* "With the majority of patients achieving MRD-negativity, and median progression-free survival not reached, these data demonstrate that a single infusion has the potential to elicit deep and durable responses in a heavily pre-treated patient population."

The study included patients (n=97) who received a median of six prior treatment regimens (range, 3-18).[1] All patients were triple-class (IMiD, PI and 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.[4]

No new safety signals were observed with longer follow-up.[2] The most common haematologic adverse events (AEs) observed were neutropenia (96 percent); anaemia (81 percent); thrombocytopenia (79 percent); leukopenia (62 percent); and lymphopenia (54 percent).[2] Since the primary 12-month publication, no new events or changes in incidence rate, time to onset, or

duration of Cytokine Release Syndrome (CRS) occurred, and one new case of treatment-related Parkinsonism, or movement and neurocognitive treatment (MNT) emergent adverse event, occurred.[1,2]

"Following the recent approval of cilta-cel in both Europe and the U.S., we are very pleased to see the latest CARTITUDE data results at nearly 28-months continuing to show the potential of CAR-T therapies for people living with relapsed/refractory multiple myeloma who otherwise have limited treatment options remaining," said Edmond Chan, MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "Now, as an approved therapeutic option, cilta-cel is testament to our ongoing commitment to invest in the areas of highest unmet need, with the ultimate aim to change what a diagnosis means for patients and their families."

Cilta-cel Results in Earlier Lines of Treatment

Findings from Cohort B (n=19) of the Phase 2 CARTITUDE-2 (NCT04133636) study,[5] evaluating the safety and efficacy of cilta-cel in patients with relapsed or refractory multiple myeloma who received one prior line of therapy including a PI and IMiD and had disease progression within 12 months of treatment with autologous stem cell transplant (ASCT), or within 12 months of the start of anti-myeloma therapy for patients who have not had ASCT, showed patients treated with cilta-cel experienced early and deep responses at a median follow-up of 13-months.[6] In 19 patients treated in this cohort, the ORR was 100 percent (95 percent CI, 82.4 to 100), with 90 percent (95 percent CI, 66.9 to 98.7) of patients achieving a CR or better and 95 percent (95 percent CI, 74.0 to 99.9) of patients achieving a very good partial response (VGPR) or better.[6] Median time to first response was one month (range, 0.9-9.7).[6] The 12-month PFS rate was 90 percent.[6] The overall safety profile, including incidence of CRS and most common haematologic AEs, was consistent with observations in the CARTITUDE-1 study.[6] These data were presented for the first time at ASCO (Abstract #8029) and will be featured as an oral presentation at the European Hematology Association (EHA) 2022 Congress (Abstract #S185).[6,7]

Updated results from Cohort A (n=20) of the CARTITUDE-2 study evaluating cilta-cel safety and efficacy in multiple myeloma patients who are lenalidomide refractory with 1–3 prior lines of treatment were also presented as a poster presentation at ASCO 2022 (Abstract #8020).[8]

"We are pleased to see the clinical benefit of cilta-cel as demonstrated in these results from CARTITUDE-1 that show deep and durable responses were maintained over time," said Sen Zhuang M.D., Ph.D., Vice President, Clinical Research and Development, Janssen Research & Development,

LLC. "As part of our dedication to advance the science of multiple myeloma, we remain committed to further investigating the potential of cilta-cel in earlier lines of treatment, including in the CARTITUDE-2 study as part of the CARTITUDE clinical development programme."

Cilta-cel received approval from the European Commission (EC) in May 2022 for the treatment of adults with relapsed and refractory multiple myeloma who received at least three prior therapies, including an IMiD, a PI and an anti-CD38 monoclonal antibody .[9] Cilta-cel has also previously received U.S. Food and Drug Administration (FDA) approval in February 2022.[10] Cilta-cel is not currently approved in any other treatment setting.

#ENDS#

About Ciltacabtagene Autoleucel (cilta-cel)

Cilta-cel is a BCMA-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T-cells with a transgene encoding a chimeric antigen receptor (CAR) that identifies and eliminates cells that express BCMA.[1,11] BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B-cells and plasma cells.[12,13] The cilta-cel CAR protein features two BCMA-targeting single domain antibodies designed to confer high avidity against human BCMA. Upon binding to BCMA-expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells.[14]

In December 2017, Janssen Biotech, Inc. (Janssen) entered into an exclusive worldwide license and collaboration agreement with Legend Biotech USA, Inc. to develop and commercialise cilta-cel.[15]

In addition to United States (U.S.) Breakthrough Therapy Designation granted in December 2019,[16] cilta-cel received a PRIority MEdicines (PRiME) designation from the EC in April 2019,[17] and a Breakthrough Therapy Designation in China in August 2020.[18] Janssen also received Orphan Drug Designation for cilta-cel from the EC in February 2020 and from the Pharmaceuticals and Medicinal Devices Agency (PMDA) in Japan in June 2020.[19] In May 2022, the Committee for Orphan Medicinal Products recommended by consensus that the orphan designation for cilta-cel be maintained, on the basis of clinical data demonstrating improved and sustained complete response rates following treatment.[20]

About the CARTITUDE-1 Study

CARTITUDE-1 (NCT03548207)[21] is an ongoing Phase 1b/2, open-label, multi-centre study evaluating cilta-cel for the treatment of patients with RRMM, have received ≥3 prior lines or who are double refractory to an IMid and PI and who have received a PI, an IMiD and an anti CD38 as part of previous therapy. Patients in the study had received a median of six prior treatment regimens (range, 3-18).[1] Of the 97 patients enrolled in the trial, 99 percent were refractory to the last line of treatment and 88 percent were triple-class refractory, meaning their cancer did not respond to, or had progressed on, an IMiD, a PI and an anti-CD38 monoclonal antibody.[4]

About the CARTITUDE-2 Study

CARTITUDE-2 (NCT04133636)[5] is an ongoing, multi-cohort Phase 2 study evaluating the safety and efficacy of cilta-cel in patients with multiple myeloma.[6] Cohort B evaluates patients who received one line of prior therapy including a PI and an IMiD, and had disease progression per IMWG criteria within 12 months after treatment with autologous stem cell transplantation (ASCT) or from the start of anti-myeloma therapy for participants who have not had an ASCT.[6] Cohort A evaluates patients who had progressive multiple myeloma after 1–3 prior lines of therapy, including a PI and an IMiD, were lenalidomide refractory, and had no prior exposure to BCMA-targeting agents.[6]

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that affects some white blood cells called plasma cells, which are found in the bone marrow.[22] In multiple myeloma, cancerous plasma cells rapidly spread and replace normal cells in the bone marrow with tumors.[14] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,500 patients died.[23] While some people diagnosed with multiple myeloma initially have no symptoms, most patients are diagnosed due to symptoms that can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, kidney problems or infections.[24]

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 & Retina; 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 Pharmaceutica NV, Janssen Biotech, Inc., Janssen-Cilag Limited and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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**Maria-Victoria Mateos, M.D., Ph.D., has been a paid consultant to Janssen; she has not been paid for contributing to this press release.*

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 Pharmaceutica NV, Janssen Biotech, Inc., Janssen-Cilag Limited and Janssen Research & Development, LLC, and 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 January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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 Janssen Biotech, Inc., Janssen Research & Development, LLC, 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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June 2022

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