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News Release

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CARVYKTI®▼ (ciltacabtagene autoleucel; cilta-cel) Reduces Risk of Disease Progression or Death by 74 Percent in Earlier-Line Multiple Myeloma Treatment in the Landmark Phase 3 CARTITUDE-4 Study

At 16 months median follow-up, cilta-cel significantly improved progression-free survival compared to two standard of care treatment regimens[1]

Data presented at the 2023 ASCO Annual Meeting and EHA Congress and published in The New England Journal of Medicine[2]

BEERSE, Belgium, 5 June 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that results from the Phase 3 CARTITUDE-4 study showed CARVYKTI®▼ (ciltacabtagene autoleucel; cilta-cel) reduced the risk of disease progression or death by 74 percent compared to two standard of care treatment (SOC) regimens, pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd), in adults with relapsed and lenalidomide-refractory multiple myeloma who received one to three prior lines of therapy.[1,3]

These data were featured in the press programme and as an oral presentation in a special session at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #LBA106), taking place in Chicago, from 2-6 June and were simultaneously published in *The New England Journal of Medicine.*[2] The results will also be presented as part of the plenary

session on Saturday 10 June, at the European Hematology Association (EHA) Hybrid Congress (Abstract #S100), taking place 8-11 June in Frankfurt, Germany. The CARTITUDE-4 study is the first randomised study investigating the efficacy of a cell therapy as early as after first relapse in multiple myeloma.[4,5]

"Results from the CARTITUDE-4 study are highly encouraging as they demonstrate significant improvements in progression-free survival, response rates and a reduction in the risk of death with cilta-cel compared to existing standards of care," said Professor Jesús San Miguel,† Director of Clinical & Translational Medicine, Universidad de Navarra, Spain. "The findings confirm the potential for cilta-cel to become a key therapy for patients with multiple myeloma earlier in their treatment journey, where unmet needs for novel therapeutic approaches remain."

The Phase 3 CARTITUDE-4 study included patients (n=419) who received one to three prior lines of therapy, including a proteasome inhibitor (PI) and immunomodulatory agent (IMiD), and were lenalidomide-refractory.[1] Patients were randomised [cilta-cel, n=208; SOC, n=211] and those in the cilta-cel arm then underwent apheresis.[1] In the cilta-cel arm, 50 percent of patients were refractory to treatment with a PI and 23 percent were refractory to treatment with anti-CD38 therapies; in the SOC group, 46 percent and 21 percent of patients were refractory to PI and anti-CD38 therapies, respectively.[1] Thirty-three percent of patients in the cilta-cel group received one prior line of treatment, compared to 32 percent of patients in the SOC group.[1]

At a median follow-up of 16 months, a 74 percent (Hazard Ratio [HR]=0.26; 95 percent Confidence Interval [CI], 0.18–0.38; p value p<0.0001) reduction in the risk of disease progression or death was observed in patients randomised to the cilta-cel arm compared to SOC.[1,3] Among patients in the cilta-cel arm, median progression-free survival (PFS) was not reached and in the SOC arm, median PFS was 11.8 months.[1] PFS at 12 months for patients in the cilta-cel arm and SOC arm was 76 percent (95 percent CI, 69 to 81) and 49 percent (95 percent CI, 42 to 55), respectively.[1,3] At the data cut-off, patients randomised to the cilta-cel arm achieved an 85 percent overall response rate (ORR) and 73 percent achieved a complete response (CR) or better.[1] Among patients in the SOC arm, the ORR was 67 percent and CR or better was 22 percent.[1] In 144 patients in the cilta-cel arm and 101 patients in the SOC arm evaluable for minimal residual disease (MRD) status, 88 percent of

patients randomised to the cilta-cel arm and 33 percent of patients randomised to the SOC arm achieved MRD negativity at the 10^{-5} threshold, respectively.[1]

No new safety signals were observed in the study. Ninety-seven percent and 94 percent of patients reported grade 3 or 4 adverse events (AEs), including infections (27 percent, 25 percent) and cytopenias (94 percent, 86 percent), respectively.[1,3] In the cilta-cel arm, 76 percent reported cytokine release syndrome (one percent grade 3, no grade 4 or 5), five percent reported immune effector-cell associated neurotoxicity syndrome (all grade 1 or 2) and one patient had a grade 1 movement and neurocognitive treatment-emergent AE (TEAE).[1,3] Overall, 39 patients in the cilta-cel arm and 46 patients in the SOC arms died; 10 cilta-cel and five SOC patients died due to TEAEs.[1]

"The results from the CARTITUDE-4 study clearly demonstrate the efficacy of cilta-cel when administered earlier in a patient's treatment journey," said Jordan Schecter, M.D., Vice President, Clinical Development Cellular Therapy Program, Janssen Research & Development, LLC. "At Janssen, we are committed to advancing innovative therapies to improve outcomes for patients and cilta-cel represents an important therapy in our approach to redefine the treatment of multiple myeloma."

On 25 May 2023, Janssen submitted a Type II variation application to the European Medicines Agency (EMA) based on the CARTITUDE-4 study results seeking approval of cilta-cel for the earlier treatment of patients with relapsed and lenalidomide-refractory multiple myeloma.

Final Analysis of the CARTITUDE-1 Study of cilta-cel

Study closeout results from the Phase 1b/2 CARTITUDE-1 study (NCT03548207) of cilta-cel in adult patients with relapsed and refractory multiple myeloma who have received three or more prior lines of therapy including a PI, IMiD, and anti-CD38 antibody therapy showed at median follow up of 33.4 months, median PFS was 34.9 months (95 percent CI, 25.2 to not estimable [NE]), and median duration of response was 33.9 months (95 percent CI, 25.5-NE).[6] No new safety signals or neurotoxicity events were reported since the 27.7 month median follow-up.[6] These data were featured as a poster presentation at the 2023 ASCO Annual Meeting (Abstract #8009) and will be presented as an oral presentation at the 2023 EHA Hybrid Congress (Abstract #S202).[6]

"The latest CARTITUDE-1 and CARTITUDE-4 data reinforce the potential of a single infusion of cilta-cel, both in the heavily pretreated relapsed and refractory patient population for which it is currently approved, and in eligible patients as early as after first relapse," said Edmond Chan, MBChB M.D. (Res), Senior Director, EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "Our goal has always been to address the needs of patients at each stage of the disease, and ultimately achieve sustained remissions earlier in their treatment journey, and we are excited to be making great progress towards this ambition with cilta-cel."

#ENDS#

About Ciltacabtagene Autoleucel (cilta-cel)

Cilta-cel received conditional marketing authorisation from the European Commission in May 2022, for the treatment of adults with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an IMiD, a PI and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.[7,8] In February 2022, the U.S. Food and Drug Administration (FDA) approved cilta-cel for the treatment of adults with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 monoclonal antibody.[9,10] For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using cilta-cel please refer to the Summary of Product Characteristics for further information.[8] In line with EMA regulations for new medicines and those given conditional approval, cilta-cel is subject to additional monitoring.

Cilta-cel is a B-cell maturation antigen (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.[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.[11] The CAR-modified T-cells express fusion proteins of antigen receptors against tumour-associated surface antigens and T-cell activation domains, and upon binding to BCMA-expressing cells redirect the effector T-cells and enhance tumour-specific immunosurveillance.[14]

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

About CARTITUDE-4

CARTITUDE-4 (NCT04181827) is the first international, randomised, open-label Phase 3 study evaluating the efficacy and safety of cilta-cel versus PVd or DPd in adult patients with relapsed and lenalidomide-refractory multiple myeloma who received one to three prior lines of therapy.[1]

About CARTITUDE-1

CARTITUDE-1 (NCT03548207) is a Phase 1b/2, open-label, multi-center study evaluating cilta-cel for the treatment of patients with relapsed and refractory multiple myeloma, who previously received a PI, an IMiD and an anti-CD38 monoclonal antibody, and who had disease progression on or after the last regimen. Patients in the study had received a median of six prior treatment regimens (range, 3-18). 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.[6,16]

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[17] In multiple myeloma, these malignant plasma cells change and grow out of control.[13] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,400 patients died.[18] While some patients with multiple myeloma initially have no symptoms, others can have common signs and symptoms of the disease, which can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, or kidney failure.[19]

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 https://www.linkedin.com/company/JanssenEMEA for our latest news.

Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Research & Development, LLC and Janssen Biotech, Inc., 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 (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 materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Research & Development, LLC, Janssen Biotech, Inc., 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 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 1, 2023, 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 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.

†Professor Jesús San Miguel, Director of Clinical & Translational Medicine, Universidad de Navarra has provided consulting, advisory, and speaking services to Janssen; he has not been paid for any media work.

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