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**News Release**

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# Treatment with CARVYKTI®▼ (ciltacabtagene autoleucel) Resulted in Clinically Meaningful Improvements in Health-Related Quality of Life and Reductions in Disease-Specific Symptoms in Patients with Earlier-Line Multiple Myeloma

*Oral presentations at the 2023 ASH Annual Meeting including patient-reported outcomes from the CARTITUDE-4 study, and longer-term efficacy and safety data from CARTITUDE-2 study cohorts A and B, show the potential of ciltacabtagene autoleucel in earlier lines of treatment*[1,2]

**BEERSE, BELGIUM, 12 December, 2023** – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today new patient-reported outcomes (PROs) from the Phase 3 CARTITUDE-4 study of CARVYKTI®▼ (ciltacabtagene autoleucel; cilta-cel) that demonstrated clinically meaningful improvements in health-related quality of life and meaningful reductions in disease-specific symptoms according to multiple PRO measures in the treatment of adult patients with relapsed and lenalidomide-refractory multiple myeloma who received one to three prior lines of therapy (LOT).[1] These data were featured as an oral presentation at the 2023 American Society of Hematology (ASH) Annual Meeting (Abstract #1063), taking place in San Diego from 9-12 December.[1]

"These results from the CARTITUDE-4 study showed the potential of cilta-cel to significantly improve health-related quality of life measures for patients, including pain, fatigue and emotional functioning," said Roberto Mina, Assistant Professor, Division of Hematology, Department of Molecular Biotechnology and Health Sciences, University of Torino, Turin,

Italy.[‡] "Cilta-cel has demonstrated deep and durable responses in later lines of therapy, and these results show the potential of cilta-cel for patients with lenalidomide-refractory multiple myeloma as early as after first relapse."

In this analysis of the Phase 3 CARTITUDE-4 study, patients in the cilta-cel arm reported improved functioning and symptom reduction from baseline, while PRO scores in the standard of care (SOC) regimens, pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd) arm trended toward worsening or lower degrees of improvement from baseline for most domains and symptoms.[1] Cilta-cel exceeded clinically meaningful thresholds for average improvement in global health status (10.1 points), pain (–10.2 points) and the visual analogue scale (8.0 points) from baseline to month 12; improvements in fatigue (–9.1 points) and emotional functioning (9.5 points) neared clinically meaningful thresholds.[1] Using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30; 100-point scale), a 30-item instrument designed to measure quality of life in all cancer patients, the analysis showed that results numerically favoured cilta-cel for all other domains.[1,3] The median time until multiple myeloma symptom worsening in the cilta-cel arm was 23.7 months compared to 18.9 months in the SOC arm (Hazard Ratio [HR]= 0.42; 95 percent Confidence Interval [CI], 0.26–0.68; p value p=0.003), measured with the Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q; 5-point scale).[1]

The CARTITUDE-4 study enrolled 419 patients with lenalidomide-refractory multiple myeloma and one to three prior LOT.[1] At clinical cut-off, 99 patients in the cilta-cel arm and 66 in the SOC arm had both baseline and 12-month PRO assessments, representing data prior to progression.[1] PRO compliance rates were 100 percent at baseline and decreased with subsequent visits to 74 percent in the cilta-cel and 81 percent in the SOC arm at month 12.[1] Patients were administered EORTC QLQ-C30, EuroQoL 5-Dimension 5-Level (EQ-5D-5L; 100-point scale) and MySIm-Q questionnaires throughout the course of the study.[1] In the primary analysis of CARTITUDE-4 presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting, cilta-cel reduced the risk of disease progression or death by 74 percent (HR=0.26; 95 percent CI, 0.18–0.38; p<0.0001) compared to two SOC regimens, PVd or DPd, in adults with relapsed and lenalidomide-refractory multiple myeloma who received one to three prior LOT.[4]

"Multiple myeloma is notoriously associated with a significant burden on quality of life for patients, being lower than that of other haematological malignancies," said Edmond Chan, MBChB, M.D. (Res), Senior Director, EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "At Janssen we are committed to tackling areas of high unmet need to improve not only clinical outcomes but also the quality of life for those living with multiple myeloma."

**CARTITUDE-2: Updated Cilta-Cel Results in Earlier Lines of Treatment**

Longer-term efficacy and safety data from CARTITUDE-2 cohorts A and B were also presented in an oral presentation at ASH (Abstract #1021).[2] At a median follow-up of approximately 29 months, patients treated with cilta-cel in earlier LOT, both those with lenalidomide-refractory multiple myeloma after one to three LOT (cohort A) and those with early relapse (cohort B, a functionally high-risk population), experienced deep and durable responses.[2] In the 20 patients in cohort A and 19 in cohort B, treatment with cilta-cel resulted in overall response rates of 95 percent (complete response or better [≥CR], 90 percent) and 100 percent (≥CR, 90 percent), respectively. Median progression-free survival (PFS) was not reached in either cohort, and 24-month PFS rates were 75 percent in cohort A and 73 percent in cohort B; respective 24-month overall survival rates were 75 percent and 84 percent.[2] Cohort A provides insight into potential longer-term survival outcomes that may be expected in the Phase 3 CARTITUDE-4 study, which enrolled the same patient population.[2]

In cohort A, after a median follow-up between 17.1 and 29.9 months, haematologic treatment-emergent adverse events (TEAEs) included leukopenia (60 percent all Grade 3/4), lymphopenia (80 percent all Grade 3/4) and thrombocytopenia (80 percent; 40 percent Grade 3/4).[2] No new patients reported haematologic TEAEs in cohort B, after a median follow-up between 18.0 and 27.9 months.[2] No new chimeric antigen receptor (CAR)-T-related safety signals were observed; one additional CAR-T cell neurotoxicity of sensory loss (Grade 2) which resolved was reported in cohort B.[2] One new death (total: five) occurred in cohort A due to progressive disease and one new death (total: four) occurred in cohort B due to cardiac arrest (not treatment related).[2]

"The data presented at ASH highlight our commitment to pursue the development of cutting-edge therapies with the intent of providing clinically meaningful real-life benefits for patients, in addition to robust efficacy and safety data," said Jordan Schecter, M.D., Vice

President, Clinical Development Cellular Therapy Program, Johnson & Johnson Innovative Medicine. "These analyses add to the continued evidence from the CARTITUDE-4 study and build our confidence in the profile of cilta-cel as a potential and promising treatment option for patients with multiple myeloma whose disease recurs early."

#ENDS#

**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.[5]

**About CARTITUDE-2**

CARTITUDE-2 (NCT04133636) 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 proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), and had disease progression per International Myeloma Working Group (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 LOT including a PI and an IMiD, were lenalidomide refractory, and had no prior exposure to B-cell maturation antigen (BCMA)-targeting agents.[6]

**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 (RRMM) 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 RRMM 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.[7] In line with

EMA regulations for new medicines and those given conditional approval, cilta-cel is subject to additional monitoring.

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 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 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.[16,17] In multiple myeloma, these malignant plasma cells change and grow out of control.[16] In the European Union, it is estimated that more than 35,300 people were diagnosed with multiple myeloma in 2022, and more than 22,700 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, fatigue, high calcium levels, infections, or kidney damage.[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: Oncology, Immunology, Neuroscience, Cardiovascular, Pulmonary Hypertension, and Retina.

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Learn more at www.janssen.com/emea. Follow us at www.linkedin.com/janssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech and Janssen Research & Development, LLC are part of Johnson & Johnson.

[ǂ] *Dr. Roberto Mina has provided consulting, advisory, and speaking services to Janssen; he has not been paid for any media work.*

# # #

***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 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-Cilag Limited, Jassen Biotech, Janssen Research and Development, LLC, 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; 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 http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. None of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Janssen Research and Development, LLC, 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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## References

[1] Mina, R. Patient-Reported Outcomes in the Phase 3 CARTITUDE-4 Study of Ciltacabtagene Autoleucel Vs Standard of Care in Patients with Lenalidomide-Refractory Multiple Myeloma after 1-3 Lines of Therapy. Abstract #1063 [Oral Presentation]. Presented at the 2023 American Society of Hematology Annual Meeting.
[2] Hillengass, J. The Phase 2 CARTITUDE-2 Trial: Updated Efficacy and Safety of Ciltacabtagene Autoleucel in Patients with Multiple Myeloma and 1-3 Prior Lines of Therapy (Cohort A) and with Early Relapse after First Line Treatment (Cohort B). Abstract #1021 [Oral Presentation]. Presented at the 2023 American Society of Hematology Annual Meeting.
[3] European Organisation for Research and Treatment of Cancer (EORTC). Quality of Life Questionnaires. Available at: https://qol.eortc.org/questionnaires/. Last accessed: December 2023.
[4] Dhakal B, et al. First Phase 3 results from CARTITUDE-4: Cilta-cel versus standard of care (PVd or DPd) in lenalidomide-refractory multiple myeloma. J Clin Oncol. 2023;41;17:LBA106-LBA106
[5] ClinicalTrials.gov. A Study Comparing JNJ-68284528, a CAR-T Therapy Directed Against B-cell Maturation Antigen (BCMA), Versus Pomalidomide, Bortezomib and Dexamethasone (PVd) or Daratumumab, Pomalidomide and Dexamethasone (DPd) in Participants With Relapsed and Lenalidomide-Refractory Multiple Myeloma (CARTITUDE-4). Available at: https://clinicaltrials.gov/study/NCT04181827. Last accessed: December 2023.
[6] ClinicalTrials.gov. A Study of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy Directed Against B-cell Maturation Antigen (BCMA) in Participants With Multiple Myeloma (CARTITUDE-2). Available at: https://clinicaltrials.gov/study/NCT04133636. Last accessed: December 2023.
[7] European Medicines Agency. CARVYKTI (Ciltacabtagene Autoleucel) Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/carvykti-epar-product-information_en.pdf. Last accessed: December 2023.
[8] Janssen.com. European Commission Grants Conditional Approval of CARVYKTI® (Ciltacabtagene Autoleucel), Janssen's First Cell Therapy, for the Treatment of Patients with Relapsed and Refractory Multiple Myeloma. Available at: https://www.janssen.com/european-commission-grants-conditional-approval-carvykti-ciltacabtagene-autoleucel-janssens-first Last accessed: December 2023.
[9] JnJ.com U.S. FDA Approves CARVYKTI™ (ciltacabtagene autoleucel), Janssen's First Cell Therapy, a BCMA-Directed CAR-T Immunotherapy for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma. Available at: https://www.jnj.com/u-s-fda-approves-carvykti-ciltacabtagene-autoleucel-janssens-first-cell-therapy-a-bcma-directed-car-t-immunotherapy-for-the-treatment-of-patients-with-relapsed-or-refractory-multiple-myeloma. Last accessed: December 2023.
[10] CARVYKTI® Prescribing Information. Horsham, PA: Janssen Biotech, Inc. Available at: https://www.fda.gov/media/156560/download. Last accessed: December 2023.
[11] Martin T, et al. Ciltacabtagene Autoleucel, an Anti–B-cell Maturation Antigen Chimeric Antigen Receptor T-Cell Therapy, for Relapsed/Refractory Multiple Myeloma: CARTITUDE-1 2-Year Follow-Up. J Clin Oncol. 2022;41:1265-1274.
[12] Frerichs KA, et al. Preclinical Activity of JNJ-7957, a Novel BCMA×CD3 Bispecific Antibody for the Treatment of Multiple Myeloma, Is Potentiated by Daratumumab. Clin Cancer Res. 2020;26(9):2203-2215.
[13] Cho SF, et al. Targeting B Cell Maturation Antigen (BCMA) in Multiple Myeloma: Potential Uses of BCMA-Based Immunotherapy. Front Immunol. 2018;10(9):1821.
[14] Tai YT, Anderson KC. Targeting B-cell maturation antigen in multiple myeloma. Immunotherapy. 2015;7(11):1187-1199.
[15] JnJ.com Janssen Enters Worldwide Collaboration and License Agreement with Chinese Company Legend Biotech to Develop Investigational CAR-T Anti-Cancer Therapy. Available at: https://www.jnj.com/media-center/press-releases/janssen-enters-worldwide-collaboration-and-license-agreement-with-chinese-company-legend-biotech-to-develop-investigational-car-t-anti-cancer-therapy Last accessed: December 2023.
[16] Abdi J et al. Drug resistance in multiple myeloma: latest findings on molecular mechanisms. Oncotarget. 2013;4(12):2186-2207.
[17] American Society of Clinical Oncology. Multiple myeloma: introduction. Available at: https://www.cancer.net/cancer-types/multiple-myeloma/introduction. Last accessed: December 2023.
[18] ECIS - European Cancer Information System. Estimates of cancer incidence and mortality in 2022, by country. Multiple myeloma. Available at: https://ecis.jrc.ec.europa.eu/explorer.php?$0-0$1-All$2-All$4-1,2$3-51$6-0,85$5-2022,2022$7-7$CEstByCountry$X0_8-3$X0_19-AE27$X0_20-No$CEstBySexByCountry$X1_8-3$X1_19-AE27$X1_-1-1$CEstByIndiByCountry$X2_8-3$X2_19-AE27$X2_20-No$CEstRelative$X3_8-3$X3_9-AE27$X3_19-AE27$CEstByCountryTable$X4_19-AE27. Last accessed: December 2023.
[19] American Cancer Society. Multiple myeloma: early detection, diagnosis and staging. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8740.00.pdf. Last accessed: December 2023.