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Johnson&Johnson

Media contact:
Jenni Mildon
jmildon@its.jnj.com
+44 7920 418 552

Investor contact:
Raychel Kruper
investor-relations@its.jnj.com

For Immediate Release

CARVYKTI®▼ (ciltacabtagene autoleucel; cilta-cel) significantly improved progression-free survival and deepened responses versus two standard therapies for patients with functional high-risk multiple myeloma

73 percent reduction in risk of disease progression or death seen with cilta-cel in the CARTITUDE-4 study in a subset of patients who had early relapse after initial multiple myeloma therapy[1]

BEERSE, BELGIUM (3 June, 2024) – Janssen-Cilag International NV, a Johnson & Johnson company announced today results from a subgroup analysis of the Phase 3 CARTITUDE-4 study.[1] The data show CARVYKTI®▼ (ciltacabtagene autoleucel; cilta-cel) significantly improved progression-free survival (PFS), compared to standard therapies of pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd), for patients with lenalidomide-refractory multiple myeloma after one prior line of therapy (LOT), including patients with functional high-risk (FHR) multiple myeloma.[1] FHR was defined as progressive disease within 18 months after receiving autologous stem cell transplant (ASCT), or the start of initial frontline therapy in patients with no ASCT.[1] These data were featured as an oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place in Chicago from 31 May-4 June (Abstract #7504) and will also be shared at the 2024 European Hematology Association (EHA) Congress, taking place in Madrid from 13-16 June (Abstract #P959).[1,2]

Data from the CARTITUDE-4 study supported the recent European Commission (EC) approval of cilta-cel, the first B-cell maturation antigen (BCMA)-targeted therapy approved for the treatment of patients with relapsed and refractory multiple myeloma, as early as after first relapse.[3]

A Phase 3 CARTITUDE-4 subgroup analysis included 136 patients (cilta-cel, n=68; standard therapies, n=68) who received one prior LOT, including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), and were lenalidomide-refractory.[1] After a median follow-up of 16 months (range, 0.1-27), median PFS was not reached (NR) (95 percent Confidence Interval [CI]; not estimable [NE]-NE) among patients who received cilta-cel, compared to 17 months (95 percent CI, 11-NE) for the control arm as a second-line treatment (hazard ratio [HR]=0.35 [95 percent CI, 0.2-0.7; *p*=0.0007]).[1]

In an additional subgroup analysis of 79 patients with FHR multiple myeloma (cilta-cel, n=40; standard therapies: n=39), median PFS was NR (18-NE) with cilta-cel versus 12 months (8-NE) with standard therapies (HR=0.27 [95 percent CI, 0.1-0.6; *p*=0.0006]).[1] Patients treated with cilta-cel had deeper overall response rates (88 percent; 80 percent), complete response (CR) or better (68 percent; 39 percent), minimal residual disease (MRD) negativity (65 percent; ten percent), and longer median duration of response (mDOR) (NR [16-NE]; 16 [8-NE]) compared to those treated with standard therapies.[1]

“Patients with functional high-risk myeloma whose disease progressed during the first 18 months of initial myeloma therapy are known to have poor prognosis, yet they have not been well represented in any clinical trial,” said Luciano J Costa, M.D., Ph.D., Professor of Medicine and Director of the Multiple Myeloma Program, University of Alabama at Birmingham, and principal study investigator.‡ “This subset analysis of CARTITUDE-4 provides strong evidence that these patients greatly benefit from cilta-cel and will help healthcare professionals better understand the potential of this therapy.”

The proportion of patients with grade 3 or higher treatment emergent adverse events (TEAEs) was comparable among patients who received cilta-cel versus standard therapies as second-line treatment (96 percent, 96 percent) and those with one prior LOT and FHR multiple myeloma (100 percent, 97 percent), respectively.[1] Overall, 11 patients in the cilta-cel one

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prior LOT subgroup and 11 patients in the standard therapies one prior LOT subgroup died.[1] Of patients with FHR multiple myeloma, seven patients from the cilta-cel arm and nine who received standard therapies died.[1] Of the seven deaths in patients with one prior LOT and FHR multiple myeloma, two did not receive cilta-cel as study treatment and three received cilta-cel as subsequent therapy.[1]

“Many patients with FHR multiple myeloma from the CARTITUDE-4 subgroup analysis experienced deep and durable responses following the single infusion of cilta-cel, further supporting the potential to treat a broader patient population,” said Jordan Schecter, M.D., Vice President, Disease Area Leader, Multiple Myeloma, at Johnson & Johnson Innovative Medicine. “At Johnson & Johnson, we aspire to eliminate cancer and remain steadfast in our commitment to realising the full potential of cilta-cel to improve outcomes for patients.”

CARTITUDE-2: Cilta-cel results in patients with suboptimal response to frontline autologous stem cell transplant ± lenalidomide maintenance (Abstract #7505)

Results from Cohort D of the CARTITUDE-2 study demonstrated deep and durable responses following a single infusion of cilta-cel with or without lenalidomide maintenance.[4] This cohort evaluated patients who had a suboptimal response after ASCT frontline therapy.[4] These data were presented as an oral presentation at the 2024 ASCO Annual Meeting (Abstract #7505).[4]

At a median follow-up of 22 months, patients treated with cilta-cel (n=17) demonstrated a 94 percent overall response rate with 94 percent also achieving a CR or better.[4] Of the 15 MRD-evaluable patients, 80 percent achieved MRD negativity at 10^{-5}.[4] The mDOR was NR.[4] Eighteen-month PFS and OS rates were 94 percent each.[4] Patients in Cohort D had robust CAR-T expansion, but numerically shorter persistence compared to patients with lenalidomide-refractory multiple myeloma and one to three prior LOT (CARTITUDE-4) and heavily pretreated patients (CARTITUDE-1).[4]

All patients had grade 3 or 4 TEAEs, including any grade neutropenia (94 percent), lymphopenia (65 percent), thrombocytopenia (47 percent), leukopenia (41 percent), infections (71 percent), or cytokine release syndrome (CRS) (82 percent; median onset of eight days).[4] One patient had a secondary malignancy of grade 3 myelodysplastic syndromes (MDS).[4] No cases of movement and neurocognitive treatment-emergent (MNT) AEs/parkinsonism were observed.[4]

“Patients diagnosed with lenalidomide-refractory multiple myeloma often experience more frequent and aggressive relapses and tend to have subsequently fewer treatment options available. The disease becomes more difficult to manage as it progresses, highlighting the need for more effective therapies with unique targets, to help improve prognoses for this patient group,” said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Haematology, at Johnson & Johnson Innovative Medicine. “We are aiming to transform outcomes for patients with multiple myeloma and lead where medicine is going.”

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 pomalidomide, bortezomib and dexamethasone (PVd); or daratumumab, pomalidomide and dexamethasone (DPd), in adult patients with relapsed and lenalidomide-refractory multiple myeloma who received one to three prior lines of therapy, including a PI and an IMiD.[5] Patients were randomised to receive either a sequence of apheresis, bridging therapy, lymphodepletion and cilta-cel (n=208) or standard of care (SOC), which included PVd or DPd (n=211).[1,5] The primary outcome measure for the study is PFS, defined as the time from the date of randomisation to the date of first documented disease progression, as defined in the International Myeloma Working Group (IMWG) criteria, or death due to any cause.[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. Cohort D evaluates cilta-cel with lenalidomide maintenance in patients who achieved less than CR after ASCT frontline therapy.[6]

About Cilta-cel

In April 2024, the EC approved a Type II variation for cilta-cel for the treatment of adults with relapsed and refractory multiple myeloma who have received at least one prior therapy, including an iMID and a PI, have demonstrated disease progression on the last therapy, and are refractory to lenalidomide. In April 2024, cilta-cel was approved in the U.S. for the second-line treatment of adult patients with relapsed or refractory myeloma who have received at least one prior line of therapy including a PI, an iMID, and who are refractory to lenalidomide.

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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.[3] In line with EMA regulations for new medicines and those given conditional approval, cilta-cel is subject to additional monitoring.[3]

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 chimeric antigen receptor (CAR) that directs the CAR positive T-cells to eliminate cells that express BCMA. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells.[7,8] The cilta-cel CAR protein features two BCMA-targeting single domains 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.[9]

In December 2017, Janssen Biotech, Inc., a Johnson & Johnson company, entered into an exclusive worldwide licence and collaboration agreement with Legend Biotech USA, Inc., to develop and commercialise cilta-cel.[10]

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.[11,12] In multiple myeloma, these plasma cells continue to proliferate, accumulating in the body and crowding out normal blood cells, often causing bone destruction and other serious complications.[12] In the European Union, it is estimated that more than 35,000 people were diagnosed with multiple myeloma in 2022, and more than 22,700 patients died.[13]While some people diagnosed 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 problems.[14]

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity.

Learn more at www.janssen.com/emea. Follow us at https://www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen-Cilag International NV and Janssen Research & Development, LLC are Johnson & Johnson companies.

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 materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen Research & 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; 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 actions; 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 December 31, 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, Inc., Janssen Research & Development, LLC nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

‡Dr Luciano J Costa, M.D., University of Alabama at Birmingham, has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

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