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Johnson&Johnson

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

Investor contact:
Lauren Johnson
investor-relations@its.jnj.com

For Immediate Release

Johnson & Johnson submits application to the European Medicines Agency for DARZALEX® (daratumumab) SC-based quadruplet regimen for newly diagnosed multiple myeloma patients

Submission supported by data from the Phase 3 CEPHEUS study for the treatment of patients with newly diagnosed multiple myeloma for whom transplant is not planned as initial therapy[1]

Data showed that the daratumumab subcutaneous formulation-based quadruplet regimen significantly improved minimal residual disease (MRD)-negativity and reduced the risk of progression or death compared to standard of care regimen[1]

BEERSE, BELGIUM (10 October 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced the submission of a Type II variation application to the European Medicines Agency (EMA) seeking approval for an indication extension of DARZALEX® (daratumumab) subcutaneous (SC) formulation in combination with bortezomib, lenalidomide, and dexamethasone (D-VRd) for the treatment of adult patients with newly diagnosed multiple myeloma (NDMM).[2]

“While we’ve seen significant progress in multiple myeloma treatment, there continues to be a tremendous opportunity to improve frontline therapies and ensure we are providing patients with better long-term outcomes,” said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Hematology, Innovative Medicine, Johnson & Johnson. “The potential of this daratumumab subcutaneous-based regimen to transform outcomes for people with newly diagnosed multiple myeloma is incredibly promising, and today’s submission builds on our portfolio of Phase 3 studies aimed at elevating the standard of care for all patients in the frontline treatment setting."

This submission is supported by data from the Phase 3 CEPHEUS study, which showed 60.9 percent of patients achieved minimal residual disease (MRD)-negativity with D-VRd and the risk of progression or death was reduced by 43 percent.[1] The CEPHEUS study (NCT03652064), evaluated the efficacy and safety of D-VRd compared to VRd for NDMM patients who are transplant ineligible or for whom ASCT was not planned as initial therapy (transplant ineligible or deferred).[1,2]

The D-VRd regimen increased depth and durability of responses compared to VRd, including the primary endpoint of overall MRD-negativity rate (10^{-5}) of 60.9 percent vs 39.4 percent at a median follow-up of 58.7 months (Odds Ratio [OR], 2.37; 95 percent confidence interval [CI], 1.58-3.55; p<0.0001).[1] The sustained MRD-negativity rate favoured D-VRd (48.7 percent vs 26.3 percent; p<0.0001). The study also demonstrated that D-VRd significantly reduced the risk of progression or death by 43 percent (Hazard Ratio [HR], 0.57; 95 percent CI, 0.41-0.79; p=0.0005) vs VRd and achieved an overall complete response (CR) or better rate of 81.2 percent vs 61.6 percent with VRd (p<0.0001).[1]

The overall safety profile of D-VRd was consistent with the known safety profiles for daratumumab and VRd.[1] The most common (>10 percent) Grade 3/4 haematologic and non-haematologic adverse events with D-VRd vs VRd were neutropenia (44.2 percent vs 29.7 percent), thrombocytopenia (28.4 percent vs 20.0 percent), anaemia (13.2 percent vs 11.8 percent), peripheral neuropathies (8.1 percent vs 8.2 percent), diarrhoea (12.2 percent vs 9.2 percent), and COVID-19 (11.2 percent vs 4.6 percent).[1]

“Daratumumab SC-based therapies continue to be at the forefront of multiple myeloma research. CEPHEUS is the first registrational study with a primary endpoint of MRD-negativity, supported by key secondary endpoints such as progression-free survival, filed by Johnson & Johnson in multiple myeloma,” said Craig Tendler, M.D., Vice President, Clinical Development, Diagnostics, and Global Medical Affairs, Innovative Medicine, Johnson & Johnson. “The data from CEPHEUS add to the body of evidence for daratumumab SC in newly diagnosed multiple myeloma and, together with the results of the

PERSEUS study, demonstrate the potential benefit of this quadruplet regimen for newly diagnosed patients, regardless of transplant eligibility."

Data from the CEPHEUS study was presented as a late-breaking oral presentation (LBA –1) at the 2024 International Multiple Myeloma Society (IMS) Annual Meeting.[1]

About the CEPHEUS Study

CEPHEUS is an international, randomised, open-label, Phase 3 study comparing subcutaneous daratumumab, bortezomib, lenalidomide, and dexamethasone (D-VRd) with standard bortezomib, lenalidomide, and dexamethasone (VRd).[1,2] The trial enrolled 395 patients with newly diagnosed multiple myeloma who were either ineligible for stem cell transplantation (SCT) or for whom SCT is not planned.[1] The primary endpoint was overall Minimal Residual Disease (MRD) negativity rate.[1] The minimum age for participation was 18 years for patients in both the D-VRd arm and VRd arm, with a median patient age of 70 (range 31-80).[1] The study was conducted in 13 countries across North America, South America, and Europe.[1]

About the PERSEUS Study

The PERSEUS study is being conducted in collaboration with the European Myeloma Network (EMN) as a sponsor. PERSEUS is an ongoing, randomised, open-label, Phase 3 study comparing the efficacy and safety of D-VRd followed by D-R maintenance versus VRd followed by R maintenance in 709 patients with transplant-eligible newly diagnosed multiple myeloma.[3] The primary endpoint was PFS, and secondary endpoints included overall CR or better rate, overall MRD negativity (in patients with CR or better), and overall survival (OS).[4] The median age is 61.0 (32-70) years for patients in the D-VRd arm and 59.0 (31-70) years for patients in the VRd arm.[4] The study is being conducted in 14 countries across Europe and Australia.[4]

About Daratumumab and Daratumumab SC

Johnson & Johnson is committed to exploring the potential of daratumumab for patients with multiple myeloma across the spectrum of the disease. In August 2012, Janssen Biotech, Inc., a Johnson & Johnson company and Genmab A/S entered a worldwide agreement, which granted Johnson & Johnson an exclusive licence to develop, manufacture and commercialise daratumumab. Since launch, daratumumab has become a foundational therapy in the treatment of multiple myeloma, having been used in the treatment of more than 548,000 patients worldwide.[5] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma.[6] Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[6]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[6] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[6] Daratumumab may also have an effect on normal cells.[6] Data across ten Phase 3 clinical trials, in both the frontline and relapsed settings, have shown that daratumumab-based regimens resulted in significant improvement in progression-free survival and/or overall survival.[1,4,7,8,9,10,11,12,13,14]

For further information on daratumumab, please see the Summary of Product Characteristics at: https://www.ema.europa.eu/en/documents/product-information/darzalex-epar-product-information_en.pdf.[15]

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.[16,17] In multiple myeloma, these malignant plasma cells continue to proliferate, accumulating in the body and crowding out normal blood cells, as well as often causing bone destruction and other serious complications.[18] 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.[19] Whilst 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.[18]

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 www.linkedin.com/janssenEMEA. Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., 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 daratumumab. 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; 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 December 31, 2023, including in the sections captioned "Cautionary Note Regarding

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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.

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