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News Release

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Janssen Presents Efficacy and Subgroup Analyses from MAIA Study Showing Long-Term Results of DARZALEX® (daratumumab)-based Regimen in Newly Diagnosed, Transplant-Ineligible Multiple Myeloma

Updated analyses report on progression-free survival, minimal residual disease negativity, overall response and overall survival across patient types, regardless of age or cytogenetic risk[1,2,3]

Five-year follow-up highlights health-related quality of life data in a subgroup of frail patients[4]

BEERSE, Belgium, 12 December 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new analyses from the Phase 3 MAIA study of DARZALEX® (daratumumab) in combination with lenalidomide and dexamethasone (D-Rd), evaluating progression-free survival (PFS), minimal residual disease (MRD) negativity and overall response rate (ORR) at a median follow-up of 64.5 months, and overall survival (OS) at a median follow-up of 73.6 months in newly diagnosed transplant-ineligible (TIE) patients with multiple myeloma, regardless of patients' age and across clinically important subgroups, as well as health-related quality of life (HRQoL) among frail TIE patients.[1,2,3,4] These findings were presented in oral and poster presentations at the American Society of Hematology (ASH) 2022 Annual Meeting taking place in New Orleans, U.S., and strengthen previous data from the MAIA study across clinically relevant study endpoints and patient populations.[5]

”The treatment of multiple myeloma becomes more complex with each relapse, so it is critical for frontline therapy to achieve deep treatment responses and extend survival,” said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. “This year at ASH, 168 oral presentations and posters include daratumumab – testament to its significance in the multiple myeloma treatment paradigm. We are encouraged by the latest results from the MAIA study, which reinforce the previously presented overall survival benefit of this daratumumab-based regimen as standard of care for the treatment of patients who are transplant-ineligible."

“Initial data from the MAIA study were instrumental in establishing the D-Rd regimen as a standard of care for the treatment of patients with newly diagnosed, transplant-ineligible multiple myeloma,” said study author, Shaji Kumar, M.D.*, Consultant, Division of Hematology, Department of Internal Medicine, Mayo Clinic. “These updated findings continue to reinforce the overall survival benefit with the D-Rd regimen and provide important insights across key patient populations at varying ages and levels of cytogenetic risk.”

An updated efficacy analysis from the MAIA study reports data after 64.5 and 73.6 months of median follow-up on the primary study endpoint, PFS, and the secondary endpoints of MRD negativity, and ORR and OS (Abstract #4559).[3] Additional new post hoc efficacy analyses report on critical subgroups, including by age (Abstract #4553)[1] and by cytogenetic risk factors, including Gain(1q21) and Amp(1q21) (Abstract #3245).[2]

“Daratumumab-based combination regimens are foundational in the treatment of newly diagnosed multiple myeloma, and the data presented at ASH provide further insight into the treatment of transplant-ineligible patients with the D-Rd regimen in the frontline setting,” said Mark Wildgust, Vice President, Global Medical Affairs, Janssen Research & Development, LLC. “Building on Janssen’s deep legacy in the treatment of multiple myeloma, we remain committed to evaluating the full potential of daratumumab in combination with lenalidomide and dexamethasone to meet the unique needs of various patient populations.”

The median age of the 737 patients enrolled in the MAIA trial was 73 (range: 45 to 90) years, with 44 percent of participants over the age of 75 years. Findings from the post-hoc subgroup analysis were consistent with previously reported data from the MAIA study on age and showed D-Rd improved OS, PFS, MRD negativity, and ORR compared to Rd alone in all three age groups examined, including patients under 70 years of age, between 70 and 75 years of age, and under the age of 75.[1]

- In patients under 75 years (D-Rd, n=208; Rd, n=208) who were treated with D-Rd, median PFS was not reached vs. 37.5 months in the Rd arm (Hazard Ratio [HR]: 0.52, 95 percent Confidence Interval [CI], 0.39-0.68). MRD negativity was 36.1 percent vs. 12.0 percent (odds ratio [OR], 4.13; 95 percent CI, 2.49-6.84). The ORR was 95.2 percent vs. 81.7 percent.[1]
- In patients under 70 years of age (D-Rd, n=78; Rd, n=77) who were treated with D-Rd, median PFS was not reached vs. 39.2 months in the Rd arm (HR, 0.35; 95 percent CI, 0.21-0.56). MRD negativity was 35.9 percent vs. 11.7 percent (OR, 4.23; 95 percent CI, 1.84-9.75). The ORR was 93.6 percent vs. 80.5 percent.[1]
- Lastly, in patients aged 70 through 75 (D-Rd, n=130; Rd, n=131), who were treated with D-Rd, median PFS was reached at 61.9 months vs. 37.5 months in the Rd arm (HR, 0.64; 95 percent CI, 0.45-0.89; *P* = 0.0079). MRD negativity was 36.2 percent vs. 12.2 percent (OR, 4.07; 95 percent CI, 2.16-7.67). The ORR was 96.2 percent vs. 82.4 percent.[1]

A second analysis in key clinical subgroups (Abstract #3245) reported increased PFS, MRD negativity and ORR following treatment with D-Rd in patients 75 or older, with International Staging System (ISS) stage III disease, with high cytogenetic risk, with renal insufficiency, and with extramedullary plasmacytomas.[2] Key highlights include:

- Patients with high cytogenetic risk, defined as having one or more of the abnormalities t[4;14], t[14;16] or del17p, had a median PFS of 45.3 months following treatment with D-Rd vs. 29.3 months with Rd alone (HR, 0.57; 95 percent CI, 0.34-0.96) (D-Rd, n=48; Rd, n=44). MRD negativity was 25.0 percent compared to 2.3 percent (OR, 14.33, 95 percent CI, 1.78-115.59) and the ORR was 91.7 percent vs. 75 percent (OR, 3.67, 95 percent CI, 1.07-12.55).[2]
- Patients with Gain(1q21) or Amp(1q21) had a median PFS of 53.2 months following treatment with D-Rd vs. 32.3 months with Rd alone (HR, 0.63; 95 percent CI, 0.46-0.88) (D-Rd, n=127; Rd, n=120). MRD negativity was 33.1 percent compared to 11.7 percent (OR, 3.74, 95 percent CI, 1.92-7.30) and the ORR was 95.3 percent vs. 85 percent (OR, 3.56, 95 percent CI,1.36-9.30).[2]
- The rates of Grade 3/4 and serious treatment-emergent adverse events (TEAEs) were similar in both treatment groups for patients 75 years of age or older, with a lower rate of discontinuation due to TEAEs for patients treated with D-Rd compared to Rd alone.[2]

In an additional analysis presented from the MAIA study, patient-reported outcomes (PRO) data were highlighted in an oral presentation, and showed sustained improvements in HRQoL and physical functioning among a subgroup of frail patients treated with D-Rd compared to Rd, with a notable reduction in pain throughout the duration of treatment (Abstract #472).[4] A higher percentage of patients continued treatment with D-Rd, compared to those receiving Rd alone.[4]

#ENDS#

About the MAIA Trial

The randomised, open-label, multicentre Phase 3 study included 737 newly diagnosed patients with multiple myeloma ineligible for high-dose chemotherapy and autologous stem cell transplant (ASCT), aged 45-90 years (median age of 73).[5] Patients were randomised to receive either D-Rd or Rd alone in 28-day cycles. In the D-Rd arm, patients received daratumumab 16 milligrams per kilogram (mg/kg) IV weekly for cycles 1 – 2, every two weeks for cycles 3 – 6 and every four weeks for cycle 7 and thereafter.[5] Patients in the D-Rd and Rd treatment arms received 25 mg of lenalidomide on days 1 – 21 of each 28-day cycle, and dexamethasone at 40 mg once a week for each cycle. Patients in both treatment arms continued until disease progression or unacceptable toxicity.[6]

Earlier results from the MAIA study supported the European Medicines Agency (EMA) approval of daratumumab in combination with Rd. These data were also published in *The New England Journal of Medicine* in 2019. An updated OS analysis was published in *The Lancet Oncology* in 2021.

About daratumumab and daratumumab SC

Janssen is committed to exploring the potential of daratumumab for patients with multiple myeloma across the spectrum of the disease. Daratumumab has been approved in eight indications for multiple myeloma, three of which are in the frontline setting, including newly diagnosed patients who are transplant-eligible and ineligible.[7]

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license 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 300,000 patients worldwide.[8] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma.[7] Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[9]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[7] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[7] Daratumumab may also have an effect on normal cells.[7] Data across eight

Phase 3 clinical trials, in both the frontline and relapsed settings, have shown that daratumumab based regimens resulted in significant improvement in PFS and/or OS.[10,11,12,13,14,15,16,17]

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.

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.[18] In multiple myeloma, these malignant plasma cells change and grow out of control.[9] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,400 patients died.[19] While some patients with multiple myeloma initially have no symptoms, others can have common symptoms of the disease which can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels or kidney failure.[20]

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-Cilag Limited and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

** Shaji Kumar, M.D. has served as a consultant 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 DARZALEX® (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 materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Research & Development, LLC, Janssen Biotech, Inc., 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 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 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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