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News Release

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Janssen Presents Updated Data at EHA for Teclistamab in Patients with Relapsed or Refractory Multiple Myeloma

Data show a combination of teclistamab (BCMAxCD3 bispecific antibody) plus DARZALEX® (daratumumab) subcutaneous (SC) formulation improved clinical efficacy in heavily pretreated patients with relapsed or refractory multiple myeloma[1]

BEERSE, Belgium, 10 June 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced updated efficacy and safety results from the teclistamab cohort of the Phase 1b TriMM-2 study (NCT04108195).[1] Teclistamab, an investigational, off-the-shelf, T-cell redirecting bispecific antibody targeting B-cell maturation antigen (BCMA) and CD3 on T-cells, is being studied in combination with the anti-CD38 monoclonal antibody, DARZALEX® (daratumumab) subcutaneous (SC) formulation, in patients with relapsed or refractory multiple myeloma (RRMM) who have received three or more prior lines of therapy.[1] Patients in the study, including a high proportion with prior anti-CD38 monoclonal antibody exposure, achieved encouraging overall response rates (ORR) with this combination treatment.[1] These data will be presented at the 2022 European Hematology Association (EHA) Annual Congress as an oral presentation on Sunday, 12 June (Abstract S188).

At a median follow-up of 8.6 months (range, 0.3-19.6), 76.5 percent (39/51) of response-evaluable patients enrolled in the study achieved a response, including 36 patients (70.6 percent) who achieved a very good partial response (VGPR) or better.[1] In patients with prior anti-CD38 monoclonal antibody exposure, an ORR of 73.7 percent was achieved.[1] The median time to first confirmed response was one month, and

responses remained durable and deepened over time.[1] At the analysis cut-off, 66.7 percent of patients who achieved a response (26/39) were alive and continuing on therapy.[1]

"Responders to the combination of teclistamab plus subcutaneous daratumumab included patients with prior exposure to BCMA or anti-CD38 targeted agents, which is encouraging," said Paula Rodríguez-Otero†, M.D., Ph.D., Department of Hematology, Clínica Universidad de Navarra, Pamplona, Spain and principal study investigator. "These data also suggest this steroid-sparing regimen may lead to a clinically efficacious regimen in highly refractory patients."

The open-label, multicentre, multicohort Phase 1b TriMM-2 study is investigating the safety and efficacy of teclistamab in combination with daratumumab SC for patients with RRMM.[1] Enrolled patients received a median of five prior lines of therapy, 58.5 percent were triple-class refractory, 30.8 percent were penta-drug refractory, and 63.1 percent were refractory to anti-CD38 treatment.[1] Eighty percent of patients were refractory to their last line of therapy.[1]

As of April 6, 2022, 65 patients received daratumumab SC 1,800mg at the approved schedule plus teclistamab 1.5mg/kg weekly (QW) or 3mg/kg every other week (Q2W) subcutaneously.[1] Pre-medications, including steroids, were limited to the two step-up doses and the first full dose of teclistamab.[1] Treatment with the combination regimen were tolerable and no unexpected or overlapping toxicities were observed.[1] The most common adverse events (AEs) were cytokine release syndrome (CRS) (67.7 percent, all Grade 1 or 2); neutropenia (49.2 percent, 41.5 percent Grade 3 or 4); and anaemia (41.5 percent, 27.7 percent Grade 3 or 4).[1] One patient (two percent) had Grade 1 immune effector cell–associated neurotoxicity syndrome (ICANS) which fully resolved.[1] Infections were experienced by 67.7 percent of patients (27.7 percent Grade 3 or 4).[1] Four patients died from AEs, all unrelated to teclistamab or daratumumab SC treatment.[1]

"For nearly 20 years, we have been committed to overcoming multiple myeloma and an important part of our strategy is to continue to invest and develop complementary and combinable regimens that improve outcomes for patients and their caregivers," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "Daratumumab has become a foundational therapy for multiple myeloma, and it is exciting to see how we can continue to grow its potential through combinations with novel treatments."

Pharmacodynamic analyses demonstrate that the combination upregulates CD38+/CD8+ T-cells and proinflammatory cytokines, suggesting the potential for complementary activity.[1] Additional studies are needed to fully understand the potential clinical benefit of this biological activity.

The efficacy and pharmacodynamic profile of teclistamab in combination with daratumumab SC in patients refractory to anti-CD38 therapy suggest that higher response rates may be observed in patients with anti-CD38 naïve or sensitive disease who are enrolling in the MajesTEC-3 study (NCT05083169).[1,2] The ongoing Phase 3 MajesTEC-3 study compares the efficacy of the teclistamab-daratumumab combination with daratumumab SC in combination with pomalidomide and dexamethasone (DPd) or daratumumab SC in combination with bortezomib and dexamethasone (DVd).[2] Patients in the trial must have received one to three prior lines of therapy including a proteasome inhibitor (PI) and lenalidomide; patients who have received only one prior line of therapy must be refractory to lenalidomide.[2] Patients who have progressed on or within 60 days of the last dose of lenalidomide given as maintenance therapy are also included.[2]

"These data suggest the potential of a fully immune-based regimen for patients with heavily pretreated multiple myeloma," said Yusri Elsayed, M.D., M.HSc., Ph.D., Vice President, Disease Area Leader, Hematologic Malignancies, Janssen Research & Development, LLC. "We are committed to the ongoing development of this combination and other treatments for patients who remain in need of new options."

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About Teclistamab

Teclistamab is an investigational, fully humanised, T-cell redirecting, IgG4 bispecific antibody targeting both BCMA (B-cell maturation antigen) and CD3, on T-cells.[1] BCMA is expressed at high levels on multiple myeloma cells.[3,4,5,6,7] Teclistamab redirects CD3-positive T-cells to BCMA-expressing myeloma cells to induce killing of tumor cells.[8]

Teclistamab is currently being evaluated in several monotherapy and combination studies.[9,10,11,12,13] In 2020, the European Commission (EC) and the United Stated (U.S.) Food and Drug Administration (FDA) both granted teclistamab Orphan Drug Designation for the treatment of multiple myeloma. In January 2021 and June 2021, teclistamab received a PRIority MEdicines (PRIME) designation by the European Medicines Agency (EMA) and Breakthrough Therapy Designation (BTD) by the U.S. FDA, respectively. PRIME offers enhanced interaction and early dialogue to optimise drug development

plans and speed up evaluation of cutting-edge, scientific advances that target a high unmet medical need.[14] The FDA grants BTD to expedite the development and regulatory review of an investigational medicine that is intended to treat a serious or life-threatening condition based on preliminary clinical evidence that demonstrates the drug may have substantial improvement in at least one clinically significant endpoint over available therapy.[15] In December 2021, Janssen submitted a Biologics License Application (BLA) to the FDA seeking approval of teclistamab for the treatment of patients with RRMM; a marketing authorisation application (MAA) was submitted to the EMA for teclistamab approval in January 2022.

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.[16]

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 274,000 patients worldwide.[17] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma. Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[18]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[16] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[16] Daratumumab may also have an effect on normal cells.[16] 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.[19,20,21,22,23,24,25,26]

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.[27] In multiple myeloma, cancerous plasma cells change and grow out of control.[27] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,500 patients died.[28] While some patients with multiple myeloma initially have no symptoms, most patients are diagnosed due to symptoms, which can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels or kidney failure.[29]

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

[†]Dr. Paula Rodríguez-Otero has served as a paid consultant to Janssen; she has not been paid for any media work.

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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 teclistamab and DARZALEX® (daratumumab) subcutaneous (SC) formulation. 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 Biotech, Inc., Janssen-Cilag Limited, Janssen Research & Development, LLC or 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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