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News Release

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Janssen Presents Updated Results Evaluating GPRC5D Bispecific Antibody Talquetamab in Heavily Pretreated Patients with Multiple Myeloma

Updated results for talquetamab monotherapy and in combination with DARZALEX® (daratumumab) subcutaneous (SC) formulation highlighted in oral presentations at the 2022 EHA Annual Congress[1,2]

BEERSE, Belgium, 10 June 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced updated results from the Phase 1 MonumenTAL-1 first-in-human dose-escalation study of talquetamab (NCT03399799), an investigational, off-the-shelf, T-cell redirecting bispecific antibody targeting both GPRC5D, a novel multiple myeloma target, and CD3 on T-cells.[1,3] Results from the study showed encouraging responses in heavily pretreated patients with relapsed or refractory multiple myeloma (RRMM) who received talquetamab at the recommended subcutaneous (SC) Phase 2 dose (RP2D) administered weekly (QW) or every two weeks (Q2W).[1] These data will be featured during the 2022 European Hematology Association (EHA) Annual Congress as an oral presentation on Saturday, June 11 (Abstract S182) and were recently presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #8015).

The primary objectives of the MonumenTAL-1 study were to identify the RP2D (part 1) and assess the safety and tolerability of talquetamab at the recommended dose (part 2).[1] As of April 6, 2022, 130 patients with multiple myeloma who had relapsed or were refractory or intolerant to established therapies have received talquetamab in the study.[1] For part 2, 30 patients received the weekly RP2D of 405 µg/kg QW dosing schedule following step-up doses; 100 percent were triple-class exposed, 80 percent were penta-drug exposed, 76.7 percent were triple-class refractory, 20 percent were penta-drug

refractory, and 30 percent had prior B-cell maturation antigen (BCMA)-directed therapy.[1] Forty-four patients received the RP2D of 800 µg/kg Q2W; 97.7 percent were triple-class exposed; 68.2 percent were penta-drug exposed, 77.3 percent were triple-class refractory, 27.3 percent were penta-drug refractory, and 27.3 percent had prior BCMA-targeted therapy.[1]

The overall response rate (ORR) to talquetamab treatment was consistent across both doses.[1] With a median follow-up of 13.2 months (range, 1.1-24), 70 percent (21/30) of response-evaluable patients treated with the 405 µg/kg QW dose achieved a response, 56.7 percent achieved a very good partial response (VGPR) or better, 6.7 percent achieved a complete response (CR), and 23.3 percent achieved a stringent complete response (sCR).[1] With a median follow-up of 7.7 months (range, 0.7-16), 63.6 percent (28/44) of response-evaluable patients treated with the 800 µg/kg Q2W dose achieved a response, 56.8 percent achieved a VGPR or better, 11.4 percent achieved a CR, and 9.1 percent achieved an sCR.[1] The median duration of response (DOR) was 10.2 months (95 percent Confidence Interval (CI): 3.0–not estimable) with the 405 µg/kg QW dose and 13.0 months (95 percent CI: 5.3–not estimable) with the 800 µg/kg Q2W dose.[1]

Among response-evaluable patients who were triple-class refractory, a response was achieved by 65.2 percent (15/23) of patients treated with the 405 µg/kg QW dose and 67.6 percent (23/34) of patients treated with the 800 µg/kg Q2W dose.[1] In patients who were penta-drug refractory, 83.3 percent (5/6) of patients treated with the 405 µg/kg QW dose and 75 percent (9/12) of patients treated with the 800 µg/kg Q2W dose achieved a response.[1]

"Patients with multiple myeloma who are heavily pretreated need new options," said Monique Minnema, M.D., Professor, Department of Hematology, University Medical Center, Utrecht, Netherlands, and principal study investigator.[†] "The continued deep and durable responses and tolerable safety profile seen in these longer-term data suggest that at both doses, talquetamab may offer a new treatment option for relapsed or refractory patients."

No new safety signals were identified with longer follow-up of either dose cohort (405 µg/kg QW and 800 µg/kg Q2W).[1] The most common adverse events (AEs) at the 405 µg/kg QW dose were cytokine release syndrome (CRS; 76.7 percent; 3.3 percent Grade 3/4), neutropenia (66.7 percent; 60 percent Grade 3/4), skin-related AEs (66.7 percent; all Grade 1/2), and dysgeusia (63.3 percent; all Grade 1/2).[1]

The most common AEs at the 800 µg/kg Q2W dose were CRS (79.5 percent; all Grade 1/2), skin-related AEs (72.7 percent; 2.3 percent Grade 3/4), and dysgeusia (56.8 percent).[1] Dysgeusia (altered sense of taste) was managed with supportive care and, if needed, dose adjustments.[1] Cytopenias were mostly confined to step-up doses and cycles one and two and generally resolved within one week.[1] Infections occurred in 46.7 percent (6.7 percent Grade 3/4) of patients at the 405 µg/kg QW dose and 38.6 percent (9.1 percent Grade 3/4) at the 800 µg/kg Q2W dose.[1]

Step-up dosing was used to mitigate against severe CRS, and pre-treatment medications (including steroids) were limited to the step-up and first full doses.[1]

"With additional follow-up, these data demonstrate potential durability of talquetamab responses," said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Research and Development, Janssen Research & Development, LLC. "We look forward to fully understanding the potential of this bispecific for relapsed and refractory patients through ongoing clinical development."

Updated data from the Phase 1b TriMM-2 Study Evaluating Talquetamab in Combination with DARZALEX® (Daratumumab) SC (Abstract S183)

Additional data for talquetamab will be featured in an oral presentation at EHA on Saturday, June 11 (Abstract S183).[2] The Phase 1b TriMM-2 study (NCT04108195) evaluated talquetamab in combination with daratumumab SC, the CD38-directed monoclonal antibody approved to be given subcutaneously for the treatment of patients with multiple myeloma.[2] Results from the study show that heavily pretreated patients with multiple myeloma treated with the combination, including talquetamab at the RP2D administered QW or Q2W, achieved high rates of responses, including for patients refractory to anti-CD38 treatment.[2]

The primary objectives of the TRiMM-2 study were to identify the RP2D for each component of the treatment combination (Part 1); characterise the safety of the treatment combination at the RP2D (Part 2); and assess antitumour activity, pharmacokinetics and pharmacodynamics for the combination treatment (Part 3).[2] Patients in the study (n=58) had received a minimum three prior lines of therapy or were double refractory to a proteasome inhibitor (PI) and an immunomodulatory agent; patients who had been exposed or refractory to an anti-CD38 therapy more than 90 days prior to the start of the trial were also included, as well as those refractory to anti-CD38 therapy.[2]

Patients received step-up doses of talquetamab followed by 400 µg/kg QW treatment (n=14) or 800 µg/kg Q2W treatment (n=44), in combination with daratumumab SC at the approved dosing schedule.[2] With a median follow-up of 5.1 months, the ORR was 80.4 percent (41/51) among all response-evaluable patients.[2] Of these patients, 62.7 percent (32/51) achieved a VGPR or better, and 29.4 percent (15/51) achieved a CR or better.[2] Among patients with prior exposure to an anti-CD38 antibody, the ORR was 77.3 percent (34/44), and the ORR was 72 percent (18/25) among patients with prior BCMA-targeted treatment.[2]

No new safety signals were identified with longer follow-up of either dose cohort, and the safety profile for the combination was comparable to each agent as a monotherapy.[2] The most common nonhaematologic AEs at the 400 µg/kg QW dose were CRS (71.4 percent; all Grade 1/2), dysgeusia (71.4 percent; N/A) and dry mouth (71.4 percent; all Grade 1/2).[2] The most common AEs at the 800 µg/kg Q2W dose were CRS (77.3 percent; all Grade 1/2), dysgeusia (59.1 percent; N/A), and anaemia (43.2 percent; 18.2 percent Grade 3/4).[2] Skin-related and nail disorders were reported in 81 percent of patients.[2] Infections were experienced by 53.4 percent of patients (17.2 percent Grade 3 or higher), and one patient died of pneumonia.[2]

"The results presented today reinforce our ongoing commitment to deliver transformative treatment regimens for those living with multiple myeloma," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "We are intent on expanding our portfolio to include treatments that employ different modes of action, hit a range of cellular targets and that are complementary in the way they work together, to allow us to continue to deliver new options for patients in need."

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About Talquetamab

Talquetamab is an investigational T-cell redirecting bispecific antibody targeting both GPRC5D, a novel multiple myeloma target that does not shed over time, and CD3, on T-cells.[3] CD3 is involved in activating T-cells and GPRC5D is highly expressed on multiple myeloma cells.[4,5] Results from preclinical studies in mouse models demonstrate that talquetamab induces T-cell-mediated killing of GPRC5D-expressing multiple myeloma cells through the recruitment and activation of CD3-positive T-cells and inhibits tumour formation and growth.[3]

In January 2021, talquetamab was granted PRIority MEdicines (PRIME) designation by the European Commission.

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.[6]

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.[7] 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.[8]

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 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.[9,10,11,12,13,14,15,16]

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.[17] In multiple myeloma, cancerous plasma cells change and grow out of control.[17] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,500 patients died.[18] 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.[19]

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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. Minnema has served as a 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 and 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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