News Release

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Janssen Presents Updated Results Evaluating Talquetamab (GPRC5DxCD3 Bispecific Antibody) in Heavily Pre-treated Patients with Multiple Myeloma

Updated results of weekly and biweekly dosing of talquetamab monotherapy and initial results in combination with daratumumab presented in oral presentations at the ASH 2021 Annual Meeting[1,2]

BEERSE, BELGIUM, 11 December, 2021– The Janssen Pharmaceutical Companies of Johnson & Johnson announced today updated results from the MonumenTAL-1 Phase 1 first-in-human dose-escalation study of talquetamab (NCT03399799).[1] Talquetamab is the only investigational off-the-shelf T-cell redirecting bispecific antibody in clinical development targeting both GPRC5D, a novel multiple myeloma target, and CD3 on T-cells.[1] Results from the study show that no new safety signals were observed with longer follow-up.[1] Heavily pre-treated patients with multiple myeloma treated with talquetamab at the recommended subcutaneous (SC) Phase 2 doses (RP2D) administered weekly (QW) and every two weeks (Q2W), achieved high overall responses that deepened over time.[1] These data were featured during the American Society of Hematology (ASH) 2021 Annual Meeting as an oral presentation (Abstract #158).[1]

No new safety signals were identified with longer follow-up of either dose cohort.[1] The most common adverse events (AEs) at the SC 405 µg/kg QW dose were cytokine release syndrome (CRS

– 77 percent; three percent grade 3), neutropenia (67 percent; 60 percent grade 3/4) and dysgeusia (60 percent).[1] Dysgeusia was generally mild with few dose adjustments required.[1] The most common AEs at the SC 800 µg/kg Q2W dose were CRS (72 percent; all grade 1/2), neutropenia (44 percent; 36 percent grade 3/4), and dry mouth (40 percent; all grade 1/2).[1] Cytopenias were mostly confined to step-up doses and Cycles One and Two and were reversible, including neutropenias which generally resolved within a week.[1] Infections occurred in 33 percent of patients and there was a low rate of high-grade infections (five percent grade 3/4).[1] Skin-related and nail disorder AEs occurred in 75 percent of patients, most commonly exfoliation (37 percent, at SC 405 µg/kg QW; 36 percent at 800 µg/kg Q2W, all grade 1/2), which did not lead to treatment modification.[1] Injection site reactions occurred in 16 percent of patients and were all grade 1/2.[1]

Pre-treatment medications (including glucocorticoid, antihistamine, and antipyretic treatments) were only required at the step-up and first full doses, and no steroid treatment was required after the first full dose.[1]

"New treatment options are needed for patients with multiple myeloma," said Amita Krishnan, M.D., Chief, Division of Multiple Myeloma, Department of Hematology and Hematopietic Cell Transplantation, City of Hope Comprehensive Cancer Center, Duarte, California, and principal study investigator.[*] "The continued observation of a tolerable safety profile and durable responses seen in these updated data suggest that in both doses, talquetamab may offer a new treatment option for heavily pre-treated patients."

With a median follow up of nine months (range 0.9–17.1), 70 percent (21/30) of response-evaluable patients treated with the SC 405 µg/kg QW dose achieved a response, 53 percent achieved a very good partial response (VGPR) or better, 13 percent achieved a complete response (CR) or better, and 10 percent achieved a stringent complete response (sCR).[1] With a median follow-up of 4.8 months (range 0.4–11.1), 67 percent (14/21) of response-evaluable patients treated with the SC 800 µg/kg Q2W dose achieved a response, 52 percent achieved a VGPR or better, 19 percent achieved a CR or better, and 10 percent achieved an sCR.[1] The median duration of response (DOR) was not reached for either dose.[1]

Among response-evaluable patients who were triple-class refractory, a response was achieved by 65 percent (15/23) of patients treated with the SC 405 µg/kg QW dose and 67 percent (12/18) of patients treated with the SC 800 µg/kg Q2W dose.[1] In patients who were penta-drug refractory, 83 percent (5/6) of patients responded in both dose groups.[1]

"These new data provide important insights into the potential safety, efficacy and tolerability of talquetamab for relapsed and refractory patients," said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Research and Development, Janssen Research & Development, LLC. "We look forward to fully evaluating this novel bispecific antibody as both a monotherapy and in combination immunotherapy regimens."

"Multiple myeloma remains a disease that is currently incurable, with a mortality rate that is still too high, especially for relapse and refractory patients. The updated data presented at ASH supports the potential of talquetamab as a promising new therapy to address an important unmet need," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited.

The primary objectives of the MonumenTAL-1 study were to identify the recommended subcutaneous Phase 2 dose(s) (Part 1) and assess the safety and tolerability of talquetamab at the recommended dose (Part 2).[1] As of September 2021, 102 patients with multiple myeloma who had relapsed or become refractory or intolerant to established therapies have received SC talquetamab in the study.[1] For Part 2, 30 patients received the weekly RP2D of SC 405 µg/kg QW dosing schedule with step-up doses; 100 percent were triple-class exposed, 80 percent were penta-drug exposed, 77 percent were triple-class refractory, 20 percent were penta-drug refractory and 27 percent had prior B-cell maturation antigen (BCMA)-directed therapy.[1] Twenty-five patients received the SC RP2D of 800 µg/kg Q2W; 92 percent were triple-class exposed; 68 percent were penta-drug exposed; 76 percent were triple-class refractory, 24 percent were penta-drug refractory, and 16 percent had prior BCMA-directed therapy.[1]

Data from the Phase 2 TRiMM-2 Study Evaluating Talquetamab in Combination with DARZALEX®▼ (daratumumab) subcutaneous (SC) formulation (Abstract #161)

Additional data for talquetamab will be highlighted in an oral presentation at ASH on Saturday, December 11 (Abstract #161).[2] The Phase 1b TRIMM-2 investigational 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 suggest that the combination is tolerable in patients with relapsed or refractory multiple myeloma who had received a median of six prior lines of therapy (range 2–18), with a safety profile comparable to each agent as a monotherapy at each of the three doses evaluated in the study.[2]

Patients received step-up doses of talquetamab of SC 400 µg/kg QW (n=9); SC 400 µg/kg Q2W (n=5); or SC 800 µg/kg Q2W (n=15), in combination with daratumumab SC at the approved dosing schedule.[2] At a median follow up of 4.2 months, 86 percent (6/7) of response-evaluable patients treated with the SC 400 µg/kg QW achieved a response, and 80 percent (4/5) of patients treated with the SC 400 µg/kg Q2W dose achieved a response.[2] At the SC 800 µg/kg Q2W dose of talquetamab 78 percent (7/9) of patients achieved a response.[2]

The safety profile of the combination appeared consistent with each agent as a monotherapy.[2] At all doses, the most common AE was CRS, observed in 55 percent (16/29) of patients.[2] All CRS events were grade 1/2 and all but one event occurred with step-up doses of talquetamab.[2] CRS resolved in all patients, and no patients discontinued treatment due to CRS.[2] Other AEs included dysgeusia (48 percent; all grade 1/2) and dry mouth (35 percent; all grade 1/2).[2] Skin-related and nail disorders were reported in 65 percent of patients (all grade 1/2); the most commonly reported skin or nail event was skin exfoliation (28 percent, all grade 1/2).[2] One patient experienced immune effector cell-associated neurotoxicity syndrome (ICANS), including one grade 3 event and one grade 1 event, both of which resolved but which resulted in discontinuation of talquetamab.[2]

The primary objectives of the TRiMM-2 study were to identify the Phase 2 dose (RP2D) for each component of the treatment combination (Part 1); characterise the safety of the treatment combination at the RP2D (Part 2); and assess antitumor activity, pharmacokinetics and pharmacodynamics for the combination treatment (Part 3).[2] Patients in the study (n=29) all had multiple myeloma and 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]

ENDS

About Talquetamab

Talquetamab is a first-in-class investigational bispecific antibody targeting both GPRC5D, a novel multiple myeloma target, and CD3, the T-cell receptor.[1] CD3 is involved in activating T-cells and GPRC5D is highly expressed on multiple myeloma cells.[3,4] 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.[5]

Talquetamab is currently being evaluated in a Phase 1/2 clinical study for the treatment of relapsed or refractory multiple myeloma (NCT03399799) and is also being explored in combination studies (NCT04586426).[6,7] In January 2021, talquetamab was granted PRIority MEdicines (PRIME) designation by the European Commission.[8]

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.[9]

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 227,000 patients worldwide.[10] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma (MM). Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[11]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[9] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[9] Daratumumab may also have an effect on normal cells.[9] 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.[12,13,14,15,16,17,18,19]

For further information on daratumumab, please see the Summary of Product Characteristics at: https://www.ema.europa.eu/en/medicines/human/EPAR/darzalex

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.[20] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow.[20] In Europe, more than

50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,500 patients died.[21] While some patients with multiple myeloma 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, kidney problems or infections.[22]

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

**Dr. Krishnan 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 talquetamab. 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, 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 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent 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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