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News Release

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Janssen Presents New Data for Talquetamab, a GPRC5DxCD3 Bispecific Antibody, Showing Durable Responses in Patients with Heavily Pretreated Multiple Myeloma

Results from the pivotal MonumenTAL-1 study, including first results from the Phase 2 portion, featured at the 2022 ASH Annual Meeting[1]

BEERSE, BELGIUM, 10 December 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today updated results from the Phase 1/2 MonumenTAL-1 study of talquetamab, an investigational, off-the-shelf (ready to use) bispecific T-cell engager antibody.[1,2,3] Talquetamab targets both GPRC5D, a novel target on multiple myeloma cells, and CD3 on T-cells, activating the body's immune system to fight this blood cancer.[2] Results from the study show that patients with relapsed or refractory multiple myeloma who received a median of five prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody, achieved overall response rates (ORR) of 74.1 percent and 73.1 percent with subcutaneously (SC) administered recommended Phase 2 doses (RP2Ds) of 0.4 mg/kg weekly and 0.8 mg/kg every two weeks, respectively.[1] A median duration of response (DOR) of nine months or longer was achieved in all groups, with longer DOR in those achieving a complete response (CR) or better.[1] Data from this investigational trial were featured during the 2022 American Society of Hematology (ASH) Annual Meeting, taking place in New Orleans, U.S., as an oral presentation and highlighted in an ASH press briefing on Saturday, 10 December 2022 (Abstract #157).[1,4]

"The latest results from the MonumenTAL-1 study suggest that patients are able to achieve deep and durable responses when treated with talquetamab," said Maria-Victoria Mateos, M.D., Ph.D.,

Consultant Physician in Haematology, University Hospital of Salamanca.† "These encouraging data demonstrate the potential of talquetamab as a monotherapy for patients with heavily pretreated multiple myeloma, including those who are refractory to BCMA-targeting therapies."

Results from the Phase 1 portion of the MonumenTAL-1 study were also published in *The New England Journal of Medicine* on 10 December 2022.[5]

The ORR to talquetamab treatment was similar across both dose schedules.[1] With a median follow-up of 14.9 months (range 0.5-29.0), 74.1 percent of patients treated at the SC 0.4 mg/kg dose administered weekly (QW) achieved a response, 59.4 percent achieved a very good partial response (VGPR) or better, 33.6 percent achieved a CR or better and 23.8 percent achieved a stringent complete response (sCR).[1] The median progression free survival (PFS) was 7.5 months (95 percent Confidence Interval [CI], 5.7-9.4) at the SC 0.4 mg/kg QW dose.[1] At the SC 0.8 mg/kg dose, administered every two weeks (Q2W), 73.1 percent of patients achieved a response, 57.2 percent achieved a VGPR or better, 32.4 percent achieved a CR or better, and 20 percent achieved a sCR at a median follow-up of 8.6 months (range 0.2-22.5).[1] Due to shorter follow-up in the 0.8 mg/kg Q2W dose cohort, the median PFS is not yet mature.[1] Median DOR was nine months or longer in all groups, and longer DOR was observed in those patients who achieved a CR or better.[1] There were no significant differences in ORR in subgroup analysis including prior lines of therapy, refractoriness to prior therapy and cytogenetic risk at baseline.[1]

"These data represent the importance of engaging T-cells via CD3 and targeting GPRC5D – a tumour associated antigen which is overexpressed in multiple myeloma cells – for the treatment of patients with relapsed or refractory disease," said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Research and Development, Janssen Research & Development, LLC. "We look forward to continuing our longer-term investigations of talquetamab as we aim to develop additional options for patients with this complex blood cancer."

An additional cohort was studied to determine response to talquetamab at either dose schedule after previous T-cell redirection therapy, with either a chimeric antigen receptor T-cell (CAR-T) or bispecific antibody.[1] Patients in this cohort were younger, had a higher prevalence of high-risk cytogenetics and had received a median of six prior lines of therapy (range 3.0-15).[1] Among these patients, 70.6 percent received prior CAR-T therapy and 35.3 percent received prior bispecific antibody therapy.[1] At a median follow-up of 11.8 months (range 1.0-25.4), 62.7 percent of patients with prior T-cell redirection therapy achieved a response.[1] An ORR of 72.2 percent (95

percent CI, 54.8-85.8) was observed in patients with prior CAR-T therapy and 44.4 percent (95 percent CI, 21.5-69.2) in patients with prior bispecific antibody treatment.[1] The safety profile was comparable in patients with and without prior T-cell redirection therapy.[1]

No new safety signals were identified with longer follow-up in Phase 1 or Phase 2 of the MonumenTAL-1 study.[1] The most common adverse events (AEs) at the SC 0.4 mg/kg QW dose were cytokine release syndrome (CRS) (79 percent; 2.1 percent grade 3/4), skin-related AEs (55.9 percent; all grade 1/2) and nail-related AEs (51.7 percent; all grade 1/2).[1] The most common AEs at the SC 0.8 mg/kg Q2W dose were CRS (72.4 percent; 0.7 percent grade 3/4), skin-related AEs (67.6 percent; 0.7 percent grade 3/4) and dysgeusia (distortion of the sense of taste) (46.2 percent; grade 3/4 not applicable).[1] CRS incidents were mostly grade 1/2 and largely confined to the step-up doses and first full dose.[1] The incidence of infection was 57.3 percent at the SC 0.4 mg/kg QW dose and 50.3 percent at the SC 0.8 mg/kg Q2W dose, with 16.8 percent and 11.7 percent grade 3 or higher, respectively.[1] One patient in each dose cohort died due to COVID-19 infection.[4]

Most high-grade haematologic AEs were cytopenias, which were generally limited to the first few cycles of treatment.[1] Neutropenia was observed in 34.3 percent of patients treated at the SC 0.4 mg/kg QW dose (30.8 percent grade 3/4) and 28.3 percent of patients treated at the SC 0.8 mg/kg Q2W dose (22.1 percent grade 3/4).[1] Thrombocytopenia was observed in 27.3 percent of patients treated at the SC 0.4 mg/kg QW dose (20.3 percent grade 3/4) and 26.9 percent of patients treated at the SC 0.8 mg/kg Q2W dose (16.6 percent grade 3/4).[1] At the SC 0.4 mg/kg QW dose, 4.9 percent of patients discontinued treatment due to AEs; 8.4 percent had dose delays and 14.7 percent had dose reductions.[1] At the SC 0.8 mg/kg Q2W dose, 6.2 percent of patients discontinued treatment due to AEs; 13.8 percent had dose delays and 6.2 percent had dose reductions.[1]

"Talquetamab is testament to our ongoing commitment to deliver novel treatment approaches for patients who have exhausted all other options," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "Building on over 20 years of dedication to multiple myeloma, we are continuing to invest in our portfolio to include potential treatment options that employ different mechanisms of action and have the potential to be complementary to existing treatments, to ensure we are able to best meet the needs of each individual patient."

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About the MonumenTAL-1 Study

The Phase 1/2 MonumenTAL-1 study (Phase 1: NCT03399799; Phase 2: NCT04634552) evaluated the efficacy and safety of talquetamab at the RP2Ds.[1,3,6] Patients in the Phase 1 study had shown progression on or intolerance to all established therapies and those in the Phase 2 portion had received three or more prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody (i.e., triple-class exposed).[1] Patients were split into two dosing cohorts: an SC 0.4 mg/kg QW cohort (n=143; median age, 67 years) and an SC 0.8 mg/kg Q2W cohort (n=145; median age, 67 years).[1]

About Talquetamab

Talquetamab is an off-the-shelf (ready to use), investigational bispecific T-cell engager antibody targeting both GPRC5D, a novel multiple myeloma target, and CD3 on T-cells.[2] GPRC5D is highly expressed on multiple myeloma cells and CD3 is involved in activating T-cells.[2,7]

Talquetamab, which is administered by subcutaneous injection, is an investigational therapy currently being evaluated in several monotherapy and combination studies.[3,8,9,10,11,12]

In addition to the EMA granting PRIority Medicines (PRIME) designation in January 2021, talquetamab received accelerated assessment from the EMA in November 2022. Talquetamab also received Breakthrough Therapy Designation from the U.S. FDA in June 2022. Janssen also received Orphan Drug Designation for talquetamab from the EMA in August 2021 and the FDA in May 2021.

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.[13,14] In multiple myeloma, these malignant plasma cells change and grow out of control.[13] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,400 patients died.[15] 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.[16]

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.

†Dr Maria-Victoria Mateos has served as a consultant to Janssen; she 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 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 materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Research & Development, LLC, 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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