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Janssen Presents Updated Data on First-in-Class Talquetamab at ASCO Suggesting Deep and Durable Responses in Heavily Pretreated Patients with Multiple Myeloma

Results from Phase 1 study of novel GPRC5DxCD3 T-cell redirecting bispecific antibody demonstrate promising clinical activity and support recommended Phase 2 dose

May 24, 2021 (RARITAN, N.J.) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today follow-up data from the MonumenTAL-1 Phase 1 first-in-human dose-escalation study of the investigational product talquetamab, the only off-the-shelf T-cell redirecting bispecific antibody in clinical development to target both GPRC5D, a novel multiple myeloma target, and CD3 on T-cells (NCT03399799).[1,2,3] With a median follow-up of more than six months, updated results in 30 patients with relapsed or refractory multiple myeloma treated with talquetamab by subcutaneous (SC) administration at the recommended Phase 2 dose (RP2D) showed an overall response rate (ORR) of 70 percent, with 60 percent of patients achieving a very good partial response (VGPR) or better among those who had received a median of six prior lines of therapy.[4] The median time to first confirmed response was one month (range, 0.2–3.8 months).[4] These data will be featured during the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting as an oral presentation on Tuesday, June 8 (Abstract #8008).[4]

"Most patients diagnosed with multiple myeloma will relapse over the course of their disease. Patients in this study had progressed, had relapsed after, or were refractory to numerous multiple myeloma therapies. There is a significant need for new treatments for multiple myeloma," said Jesus G. Berdeja, M.D., Director of Myeloma Research Sarah Cannon Research Institute, Tennessee Oncology, and principal study investigator. "We are encouraged that just six months after announcing the first talquetamab results at this dose, we already have follow-up data that suggest time to initial response is rapid (0.2–3.8 months) and a number of patient responses deepen with continuous therapy, supporting the further exploration of targeting both GPRC5D and CD3 in patients with multiple myeloma."

The MonumenTAL-1 Phase 1 study consists of two parts: dose escalation (part 1) and dose expansion (part 2). As of April 18, 2021, 184 patients with relapsed or refractory multiple myeloma had received talquetamab. Study results established the RP2D as weekly SC 405 µg/kg, with 10.0 and 60.0 µg/kg step-up doses during the first week of therapy. Patients treated at the RP2D had a median age of 61.5 years (range, 46–80 years) and had received a median of six prior lines of therapy (range, 2.0–14.0 months). Eighty-seven percent (n=26) were refractory to the last line of therapy; 77 percent (n=23) were triple-class (proteasome inhibitor [PI], immunomodulatory drug [IMiD], CD38 antibody) refractory and 20 percent (n=6) were penta-drug (2 PIs, 2 IMiDs, CD38 antibody) refractory; 27 percent (n=8) received prior B-cell maturation antigen (BCMA) therapy.

A response was observed in 70 percent of patients including 65 percent (15/23) of triple-class refractory patients and 83 percent (5/6) of penta-drug refractory patients. With a median follow-up of 6.3 months (range, 1.4–12.2 months), the median duration of response was not reached and 81 percent (17/21) of responders continued on treatment, suggesting that responses were durable and deepened over time for a significant number of responders at the RP2D.6 At the RP2D, pharmacodynamic data suggested consistent T-cell activation, and exposure was maintained over the maximum EC_{90} target level from an ex vivo cytotoxicity assay.6

The most common adverse events (AEs) at the RP2D were cytokine release syndrome (73 percent; 2 percent Grade 3), neutropenia (67 percent; 60 percent Grade 3/4), anemia (57 percent; 27 percent Grade 3/4) and dysgeusia (60 percent; all Grade 1/2). Infections were reported in 37 percent of patients (3 percent Grade 3/4), neurotoxicity was experienced in 7 percent of patients (all Grade 1/2) and skin-related AEs occurred in 77 percent of patients (27 percent with nail disorders). No dose-limiting toxicities occurred at the RP2D in part 1.6

"These new, updated efficacy and safety data suggest that talquetamab is a promising therapeutic candidate for the treatment of patients with multiple myeloma who have relapsed after multiple therapies or who are refractory to other treatments," said Sen Zhuang, M.D., Ph.D., Vice President, Oncology Clinical Research, Janssen Research & Development, LLC. "As the only investigational bispecific antibody directed against the novel target GPRC5D, we are committed to fully exploring talquetamab, including new subcutaneous dosing strategies in multiple myeloma."

Additional data for talquetamab will be highlighted in a poster at ASCO on Friday, June 4 (Abstract #8047).[5] The study evaluated soluble B-cell maturation antigen (sBCMA) in relapsed or refractory multiple myeloma patients treated with talquetamab or the bispecific antibody teclistamab (BCMAxCD3) and showed that both bispecific therapies induced changes in levels of sBCMA that correlated with clinical activity.

About Talquetamab

Talquetamab is a first-in-class, investigational T-cell redirecting bispecific antibody targeting both GPRC5D, a novel multiple myeloma target, and CD3, a T-cell receptor.[6] CD3 is involved in activating T-cells, and GPRC5D is highly expressed on multiple myeloma cells.[6,7,8] 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 that it inhibits tumor formation and growth.[8]

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).

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.[9,10] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow. In 2021, it is estimated that nearly 35,000 people will be diagnosed and more than 12,000 will die from the disease in the U.S.[11] While some patients with multiple myeloma initially have no symptoms, most patients are diagnosed due to symptoms that can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, kidney problems or infections.[12]

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. Follow us at @JanssenUS and @JanssenGlobal. Janssen Research & Development, LLC is a member of the Janssen Pharmaceutical Companies of Johnson & Johnson.

*Dr. Berdeja has served as a consultant to Janssen; he 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 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 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 behavior 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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[2] Pillarisetti *Blood* 135(15):1232.
[3] Atamaniuk *Eur J Clin Invest* 42(9):953. CD3, cluster of differentiation 3; MGUS, monoclonal gammopathy of undetermined significance; SMM, smoldering multiple myeloma.
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