Media Contacts:
Brian Kenney
Phone: +1 215-620-0111

Satu Glawe
Phone: +49 172-294-6264

Investor Relations:
Jennifer McIntyre
Office: +1 732-524-3922

U.S. Medical Inquiries:
+1 800-526-7736

Janssen Presents First Data from the Phase 1 Study of the GPRC5DxCD3 Bispecific Talquetamab in Patients with Relapsed or Refractory Multiple Myeloma

Data presented at ASH 2020 for first-in-class talquetamab support recommended Phase 2 dose with subcutaneous formulation

December 5, 2020 (RARITAN, N.J.) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today initial data for the Phase 1 first-in-human dose escalation study of talquetamab (JNJ-64407564) for the treatment of relapsed or refractory multiple myeloma (NCT03399799). Talquetamab is a first-in-class, and the only investigational bispecific antibody that targets both GPRC5D, a novel multiple myeloma target, and CD3 on T-cells. Initial results for both the subcutaneous (SC) and intravenous (IV) formulations show encouraging clinical activity against the GPRC5D target, which is highly expressed on multiple myeloma cells and associated with poor prognostic factors.[1,2,3] At the SC recommended Phase 2 dose (RP2D), the overall response rate (ORR) was 69 percent (9/13) and 39 percent achieved a very good partial response (VGPR) or better. The data will be featured during the American Society of Hematology (ASH) 2020 Annual Meeting as an oral presentation on Saturday, December 5 at 5:00 p.m. ET (Abstract #290).

"There is a pressing need for continued innovation of multiple myeloma treatments – particularly for patients who have relapsed on other therapies – and the results presented today for talquetamab are encouraging," said Ajai Chari, M.D., Professor of Medicine, the Director of Clinical Research in the Multiple Myeloma Program, and the Associate Director of Clinical Research, Mount

Sinai Cancer Clinical Trials Office. "The Phase 1 overall response rate and safety profile support further study of talquetamab in monotherapy and in combination approaches for patients with few options for treatment."

Investigators identified the RP2D of 405 µg/kg SC and concluded subcutaneous treatment may provide an opportunity for less frequent dosing than the intravenous formulation. A response was observed in 6/9 triple-class refractory patients and 2/2 penta-drug refractory patients. Pharmacokinetic results indicate target exposure levels at the RP2D. At the RP2D of 405 µg/kg SC, pharmacodynamic data demonstrate consistent T-cell activation, cytokine production and redistribution.

Patients received talquetamab at doses of 1–180 µg/kg with IV administration and 5–800 µg/kg for the SC formulation. Results from the Phase 1 study showed responses in patients who were treated with talquetamab across dose groups; median time to first confirmed response across all doses was one month (range, 0.2–3).[4]

The Phase 1 study enrolled patients (n=157) with multiple myeloma who had progressed on, or could not tolerate, any available established therapies. Patients had received a median of six prior lines of treatment (range, 2-20); 87 percent were refractory to the last line of therapy, 82 percent were triple-class refractory, and 33 percent were penta-drug refractory to two or more immunomodulatory agents, two or more PIs, and an anti-CD38 therapy. The study is conducted in two parts: dose escalation (part 1) and dose expansion (part 2).[4]

In the Phase 1 study, adverse events (AEs) at the RP2D which occurred with a Grade 3 frequency of ≥25 percent among the SC cohort were neutropenia (42 percent). With SC dosing, cytokine release syndrome (CRS) was observed in 64 percent of patients and was low-grade with no Grade 3 or greater CRS events at the RP2D. CRS occurred at a median of two days after dosing, and median duration of CRS was also two days. The incidence of neurotoxicity was five percent at the RP2D, with no patients experiencing Grade 3 or greater events with SC dosing.[4]

"GPRC5D is a novel target in the treatment of multiple myeloma and, as a bispecific antibody that engages T-cells by also targeting CD3, talquetamab is emerging as a potential therapeutic option for heavily pretreated patients," said Yusri Elsayed, M.D., MHSc., Ph.D., Vice President, Global Head, Hematologic Malignancies, Janssen Research & Development, LLC. "Based on the preliminary

efficacy, safety, pharmacokinetic and pharmacodynamic data presented today, we are committed to fully exploring the promise of talquetamab in multiple myeloma."

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.[4] CD3 is involved in activating T-cells and GPRC5D is highly expressed on multiple myeloma cells.[4,5,6] 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 tumor formation and growth.[6]

Talquetamab is currently being evaluated in a Phase 1/2 clinical study for the treatment of relapsed or refractory multiple myeloma and is also being explored in combination studies. The development of the antibody followed Janssen Biotech, Inc.'s licensing agreement with Genmab for use of its DuoBody® technology platform.*

*DuoBody® is a registered trademark of Genmab A/S.

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.[7,8] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow. In 2020, it is estimated that more than 32,000 people will be diagnosed and close to 13,000 will die from the disease in the U.S.[9] 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.[10]

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.

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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 December 29, 2019, 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. Neither 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.

[1] Smith *Sci Transl Med* 11(485):eaau7746.
[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.
[4] Chari A et al. A Phase 1, First-in-Human Study of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D (GPRC5D) x CD3 Bispecific Antibody, in Patients with Relapsed and/or Refractory Multiple Myeloma (RRMM).: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7408718/. Accessed November 2020
[5] Labrijn AF et al. Proc Natl Acad Sci USA. 2013;110:5145.
[6] Cohen, Y., et al. Hematology. 2013 Nov; 18(6):348-51.
[7] Kumar SK, et al. *Leukemia*. 2012 Jan; 26(1):149-57.
[8] American Cancer Society. "What Is Multiple Myeloma?." Available at: http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma. Accessed November 2020.
[9] American Cancer Society: Cancer Facts & Statistics. American Cancer Society | Cancer Facts & Statistics. https://cancerstatisticscenter.cancer.org/#!/cancer-site/Myeloma. Accessed November 2020.
[10] American Cancer Society. "Key Statistics About Multiple Myeloma." Available at: https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html. Accessed January 2020.