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Media Enquiries:
Noah Reymond
Mobile: +31 621-385-718
Email: NReymond@ITS.JNJ.com

Investor Relations:
Jessica Moore
Mobile: +41 79 395 4823
Email: Jmoore29@its.jnj.com

New Data from MajesTEC-1 Study Show Continued Deep and Durable Responses of Teclistamab (BCMAxCD3 Bispecific Antibody) in Treatment of Heavily Pre-treated Patients with Multiple Myeloma

Phase 1b results of teclistamab in combination with DARZALEX®▼ (daratumumab) subcutaneous (SC) also presented at ASH 2021 Annual Meeting[1,2]

BEERSE, BELGIUM, 13 December 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced the first presentation of Phase 2 data and updated Phase 1 data from the MajesTEC-1 study of teclistamab, an investigational off-the-shelf T-cell redirecting bispecific antibody, being studied for the treatment of patients with relapsed or refractory multiple myeloma.[1] With a median follow-up of nearly eight months, an overall response rate (ORR) of 62 percent was observed at the recommended SC Phase 2 dose (RP2D) of 1.5 mg/kg in heavily pre-treated patients (n=150) across the Phase 1 and 2 studies who had received at least three prior lines of therapy and were triple-class exposed.[1] Results were presented during the American Society of Hematology (ASH) 2021 Annual Meeting as an oral presentation (Abstract # 896) and selected as part of the Highlights of ASH programmme.[1]

MajesTEC-1 Data Highlights

At the median follow-up of nearly eight months, an ORR of 62 percent (93/150; 95 percent Confidence Interval [CI], range, 53.7–69.8) was observed; ORR was consistent regardless of cytogenetic risk or extent of prior therapy refractoriness.[1] At the clinical cut-off, median duration of

response was not reached and 88 percent (82/93) of responders were alive and continuing treatment.[1] Study results suggest that responses to teclistamab were durable and deepened over time.[1] Among patients who responded, the median time to first confirmed response was 1.2 months (range 0.2–5.5 months).[1]

Fifty-eight percent of patients receiving teclistamab achieved a very good partial response (VGPR) or better; 29 percent achieved a complete response (CR) or better; and 21 percent achieved a stringent complete response (sCR).[1] By intent-to-treat, 25 percent of patients (37/150) achieved minimal residual disease (MRD) negativity at a threshold of 10^{-5} (95 percent CI, range, 18.0–32.4).[1] In patients who achieved CR or better, the MRD negativity rate was 42 percent.[1] The progression-free survival (PFS) rate at nine months was 59 percent (95 percent CI, range, 48.8–67.0). Median overall survival (OS) was not reached.[1]

"Despite newly approved therapies for triple-class exposed patients with relapsed or refractory multiple myeloma, there remains a high unmet medical need," said Philippe Moreau*, M.D., Clinical Hematology, University Hospital Hôtel-Dieu, Nantes, France, and study investigator. "The objective responsive rate observed in this study suggests a potential benefit for patients with triple-class exposed disease with an off-the-shelf therapy."

As of September 2021, 165 patients were treated with teclistamab at the SC 1.5 mg/kg dose across both Phase 1 and Phase 2 of MajesTEC-1.[1] The primary objectives of the MajesTEC-1 Phase 1 study (NCT03145181) were to identify the recommended SC RP2D (Part 1) and characterise the safety and tolerability of teclistamab at the RP2D (Part 2).[3] The primary objective of the MajesTEC-1 Phase 2 study (NCT04557098) was to evaluate the efficacy of teclistamab at the RP2D, established at SC 1.5 mg/kg QW, as measured by ORR.[1]

Teclistamab had a tolerable safety profile and no patients required a dose reduction.[1] The most common non-haematologic adverse events (AEs) were cytokine release syndrome (72 percent; all grade 1/2 except for one grade 3 event that was fully resolved; all resolved with no treatment discontinuation), injection site erythema (26 percent; all grade 1/2) and fatigue (25 percent; two percent grade 3/4).[1] The most common haematologic AEs were neutropenia (66 percent; 57 percent grade 3/4), anaemia (50 percent; 35 percent grade 3/4) and thrombocytopenia (38 percent; 21 percent grade 3/4).[1] Five patients (three percent; all grade 1/2) developed immune effector cell-associated neurotoxicity syndrome (ICANS) all resolved without discontinuation.[1]

"These longer-term data suggest that heavily pre-treated patients in need of a new option may achieve sustained durable responses and high overall response rates for teclistamab," said Yusri Elsayed, M.D., M.HSc., Ph.D., Vice President, Hematologic Malignancies Disease Area Leader, Janssen Research & Development, LLC. "We remain focused on identifying new treatments for patients with relapsed or refractory multiple myeloma, including T-cell redirecting bispecific antibodies like teclistamab, for use alone and in novel immunotherapy regimens."

"Our mission is to develop transformational treatment regimens that address patient needs and offer physicians options which they have not had before," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "The data presented at ASH support the promising potential of teclistamab as an off-the-shelf T-cell redirecting therapy, for patients urgently in need of new options and innovative approaches."

TRIMM-2 Data Highlights

Additional data for teclistamab were highlighted in a poster session at ASH on Saturday, December 11 (Abstract #1647).[2] Results from the TRIMM-2 study (NCT04108195), evaluating teclistamab in combination with daratumumab SC – a CD38-directed monoclonal antibody approved to be given subcutaneously for the treatment of patients with multiple myeloma – suggest a manageable safety profile and preliminary efficacy in patients with relapsed or refractory disease who had received a minimum of three prior lines of treatment.[2]

ENDS

About Teclistamab

Teclistamab is an investigational, off-the-shelf, T-cell redirecting bispecific antibody targeting both B-cell maturation antigen (BCMA) and CD3. BCMA is expressed at high levels on multiple myeloma cells.[4,5,6,7] Teclistamab appears to redirect CD3-positive T-cells to BCMA-expressing myeloma cells to induce killing of tumour cells.[7] Results from preclinical studies demonstrate that teclistamab kills myeloma cell lines and bone marrow-derived myeloma cells from heavily pre-treated patients.[5]

Teclistamab is currently being evaluated in several monotherapy (NCT04557098)[8] and combination (NCT04586426, NCT04108195, NCT04722146, NCT05083169) studies.[9,10,11,12] In 2020, the European Commission (EC) and the United States (U.S.) Food and Drug Administration (FDA) each

granted teclistamab Orphan Drug Designation for the treatment of multiple myeloma. In January 2021 and June 2021, teclistamab received a PRIority MEdicines (PRIME) designation by the European Medicines Agency (EMA) and Breakthrough Therapy Designation (BTD) by the FDA, respectively. PRIME offers enhanced interaction and early dialogue to optimise drug development plans and speed up evaluation of cutting-edge, scientific advances that target a high unmet medical need.[13] The FDA grants BTD to expedite the development and regulatory review of an investigational medicine that is intended to treat a serious or life-threatening condition and is based on preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy.[14]

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.[15]

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.[16] 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.[17]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[15] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[15] Daratumumab may also have an effect on normal cells.[15] 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.[18,19,20,21,22,23,24,25]

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.[26] When damaged, these plasma cells rapidly spread and replace normal cells with tumours in the bone marrow.[26] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,500 patients died.[27] 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, kidney problems or infections.[28]

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. Moreau 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 the product development and the potential benefits and treatment impact of teclistamab. 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, Janssen Research & Development, LLC, Janssen-Cilag Limited and/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 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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