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Janssen's Updated Phase 1 Results for Teclistamab Suggest Deep, Durable Responses in Patients with Heavily Pretreated Multiple Myeloma

Subcutaneous administration of BCMAxCD3 T-cell redirecting bispecific antibody demonstrated clinical activity and a manageable safety profile according to new data at ASCO

BEERSE, BELGIUM, 24 May 2021– The Janssen Pharmaceutical Companies of Johnson & Johnson announced today updated results from the Phase 1 MajesTEC-1 study, the first-in-human dose-escalation study of teclistamab, an off-the-shelf T-cell redirecting bispecific antibody, in the treatment of patients with relapsed or refractory multiple myeloma (NCT03145181).[1] With a median follow-up of 6.1 months (range 1.2-12.2), an overall response rate (ORR) of 65 percent was observed at the recommended subcutaneous (SC) Phase 2 dose (RP2D) in a cohort of heavily pretreated patients (n=40) who had received a median of five prior lines of therapy.[2] These data will be featured during the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting as an oral presentation on Tuesday 8 June (Abstract #8007).[2]

Study results showed that responses were durable and deepened over time – 58 percent of patients receiving teclistamab achieved a very good partial response (VGPR) or better, and 40 percent achieved a complete response (CR) or better at the RP2D SC dose of 1500µg/kg. The median time to first confirmed response was one month.[2] The median duration of response was not reached. After a median follow-up of 7.1 months (range, 3.0–12.2 months), median duration of response was not reached and 85 percent (22/26) of responders were alive and continuing treatment.[2]

There were no dose-limiting toxicities at the RP2D in part 1 of the study. Grade 1 neurotoxicity was reported in one patient (1 percent) treated at RP2D.[2] The most common adverse events at the RP2D were cytokine release syndrome (70 percent; all Grade 1/2) and neutropenia (65 percent; 40 percent Grade 3/4). The promising safety, efficacy, pharmacokinetics and pharmacodynamics confirm the selection of the 1500 ug/kg SC as the RP2D.[2]

Forty patients were treated with the RP2D, identified as 1500 µg/kg SC.[2] Patients receiving the RP2D of teclistamab in this study had received a median of five prior lines of therapy (range 2–11);100 percent were triple-class (proteasome inhibitor [PI], immunomodulatory drug (IMiD), CD38 antibody) exposed; 65 percent (n=26) were penta-drug (2 PIs, 2 IMiDs, CD38 antibody) exposed; 83 (n=33) percent were triple-class refractory; 38 percent (n=15) were penta-drug refractory; 83 percent (n=33) were refractory to their last line of therapy.[2] Patients with triple-class refractory and penta-drug refractory multiple myeloma often experience poor survival outcomes as treatment options are limited.[3]

"We reported initial findings for teclistamab at ASCO 2020, and study updates have observed a deepening of responses that have shown to be durable in a significant percentage of patients with relapsed or refractory multiple myeloma," said Amrita Y. Krishnan, M.D., Director of the Judy and Bernard Briskin Center for Multiple Myeloma Research and Chief, Division of Multiple Myeloma, Department of Hematology and Hematopoietic Cell Transplantation at City of Hope, and study investigator*. "Teclistamab

exposure was sustained across the dosing interval and exceeded target levels, and consistent T-cell activation was observed. With this latest follow-up data, we present further evidence of promising clinical activity in heavily pre-treated patients, who are in urgent need of new therapeutic options."[2]

The primary objectives of the Phase 1 study were to identify the RP2D (part 1) and characterise the safety and tolerability of teclistamab at the RP2D (part 2).[2] As of March 2021, the study had enrolled 157 patients with multiple myeloma whose disease was relapsed, refractory, or intolerant to established therapies.[2]

"We remain committed to investigating new treatments and approaches for patients with multiple myeloma, including off-the-shelf, T-cell redirecting bispecific antibodies like teclistamab," said Yusri Elsayed, M.D., M.HSc., Ph.D., Vice President, Global Head, Hematologic Malignancies, Janssen Research & Development, LLC.. "The encouraging efficacy data reported at ASCO and the especially the durability of the deep responses support the further investigation of teclistamab use as a monotherapy and in combination with other agents."

"Despite significant treatment advances in multiple myeloma over the last decade, it remains a disease with high unmet need," said Edmond Chan, EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "These study findings are an important step forward in enabling us to address these needs and may potentially provide a valuable alternative treatment option in the future."

Additional data for teclistamab will be highlighted in a poster at ASCO on Friday 4 June (Abstract #8047).[4] The study evaluated soluble B-cell maturation antigen (sBCMA) in patients with relapsed or refractory multiple myeloma treated with teclistamab or the bispecific antibody talquetamab (GPRC5DxCD3) and showed that both bispecific therapies induced changes in levels of sBCMA that correlated with clinical activity.[4]

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About Teclistamab

Teclistamab is an investigational, t-cell redirecting bispecific antibody targeting both BCMA and CD3. BCMA, B-cell maturation antigen, is expressed at high levels on multiple myeloma cells.[5,6,7,8] Teclistamab redirects CD3-positive T-cells to BCMA-expressing myeloma cells to induce cytotoxicity of the targeted cells.[8] Results from preclinical studies demonstrate that teclistamab kills myeloma cell lines and bone marrow-derived myeloma cells from heavily pre-treated patients.[6]

Teclistamab is currently being evaluated in a Phase 2 clinical study for the treatment of relapsed or refractory multiple myeloma (NCT04557098)[9] and is also being explored in combination studies (NCT04586426, NCT04108195, NCT04722146).[10,11,12] In 2020, the European Commission and the U.S. Food and Drug Administration each granted teclistamab orphan designation for the treatment of multiple myeloma.

About Multiple Myeloma

Multiple myeloma (MM) is an incurable blood cancer that starts in the bone marrow and is characterised by an excessive proliferation of plasma cells.[13] In Europe, 50,918 people were diagnosed with MM in 2020, and more than 32,400 patients died.[14] Around 50 percent of newly diagnosed patients do not reach five-year survival,[15] and approximately 10 percent of patients with multiple myeloma will die within one year of diagnosis.[16]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[17] Refractory MM is when a patient's disease progresses on or within 60 days of their last therapy.[18] Relapsed cancer is when the disease has returned after a period of initial, partial or complete remission.[19] While some patients with MM have no symptoms at all, others are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[20] Patients who relapse after treatment with standard therapies, including protease inhibitors and immunomodulatory agents, have poor prognoses and require new therapies for continued disease control.[21]

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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*Dr. Krishnan has served as a paid 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 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 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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