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

Phase 1b results of teclistamab in combination with DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) also presented at ASH 2021 Annual Meeting

ATLANTA, Ga., December 13, 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 off-the-shelf T-cell investigational redirecting bispecific antibody, being studied for the treatment of patients with relapsed or refractory multiple myeloma. With a median follow-up of nearly eight months, an overall response rate (ORR) of 62 percent was observed at the recommended subcutaneous (SC) Phase 2 dose (RP2D) of 1.5 mg/kg in heavily pretreated 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 program.[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 cutoff, 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 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 9 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 many 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 characterize the safety and tolerability of teclistamab at the RP2D (part 2). 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.

Teclistamab had a tolerable safety profile, and no patients required a dose reduction.[1] The most common nonhematologic adverse events (AEs) were cytokine release syndrome (72 percent; all grade 1/2 except for 1 grade 3 event that fully resolved; all resolved with no treatment discontinuation), injection site erythema (26 percent; all grade 1/2) and fatigue (25 percent; 2 percent grade 3/4).[1] The most common hematologic AEs were neutropenia (66 percent; 57 percent grade 3/4), anemia (50 percent; 35 percent grade 3/4) and thrombocytopenia (38 percent; 21 percent grade 3/4).[1] Five patients (3 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 pretreated 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."

TRIMM-2 Data Highlights

Additional data for teclistamab were highlighted in a poster session at ASH on Saturday, December 11 (Abstract #1647). Results from the TRIMM-2 study (NCT04108195), evaluating teclistamab in combination with DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) – the 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]

About Teclistamab

Teclistamab is an investigational, off-the-shelf, T-cell redirecting bispecific antibody targeting both BCMA (B-cell maturation antigen) and CD3. BCMA is expressed at high levels on multiple myeloma cells.[3,4,5,6,7] Teclistamab appears to redirect CD3-positive T-cells to BCMA-expressing myeloma cells to induce killing of tumor cells.[5,6] Results from preclinical

studies demonstrate that teclistamab kills myeloma cell lines and bone marrow-derived myeloma cells from heavily pretreated patients.[6]

Teclistamab is currently being evaluated in several monotherapy (NCT04557098) and combination (NCT04586426, NCT04108195, NCT04722146, NCT05083169) studies. In 2020, the European Commission and the 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 from the European Medicines Agency (EMA) and Breakthrough Therapy Designation (BTD) by the U.S. FDA, respectively. PRIME offers enhanced interaction and early dialogue to optimize drug development plans and speed up evaluation of cutting-edge, scientific advances that target a high unmet medical need.[8] The U.S. 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.[9]

About DARZALEX *FASPRO*®

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered into a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize daratumumab. DARZALEX *FASPRO*® is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma and now light chain (AL) amyloidosis. DARZALEX *FASPRO*® is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

DARZALEX *FASPRO*® is indicated for the treatment of adult patients with multiple myeloma:

- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy

- in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- in combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- as monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

DARZALEX *FASPRO*® in combination with bortezomib, cyclophosphamide, and dexamethasone is indicated for the treatment of adult patients with newly diagnosed AL amyloidosis. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Limitations of Use

DARZALEX *FASPRO*® is not indicated and is not recommended for the treatment of patients with AL amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials.

Full prescribing information for DARZALEX *FASPRO*® is available here.

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.[10,11] 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.[12] 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.[13]

DARZALEX *FASPRO*® IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DARZALEX *FASPRO*® is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*®. Fatal reactions have been reported with daratumumab-containing products, including DARZALEX *FASPRO*®.

Systemic Reactions

In a pooled safety population of 898 patients with multiple myeloma (N=705) or light chain (AL) amyloidosis (N=193) who received DARZALEX *FASPRO*® as monotherapy or in combination, 9% of patients experienced a systemic administration-related reaction (Grade 2: 3.2%, Grade 3: 1%). Systemic administration-related reactions occurred in 8% of patients with the first injection, 0.3% with the second injection, and cumulatively 1% with subsequent injections. The median time to onset was 3.2 hours (range: 4 minutes to 3.5 days). Of the 140 systemic administration-related reactions that occurred in 77 patients, 121 (86%) occurred on the day of DARZALEX *FASPRO*® administration. Delayed systemic administration-related reactions have occurred in 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension and tachycardia. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritis, chills, vomiting, nausea, and hypotension.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen and corticosteroids. Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX *FASPRO®.* Consider administering corticosteroids and other medications after the administration of DARZALEX *FASPRO®* depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.7%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 5 minutes (range: 0 minutes to 6.5 days) after starting administration of DARZALEX *FASPRO®*. Monitor for local reactions and consider symptomatic management.

Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis

Serious or fatal cardiac adverse reactions occurred in patients with light chain (AL) amyloidosis who received DARZALEX *FASPRO®* in combination with bortezomib, cyclophosphamide and dexamethasone. Serious cardiac disorders occurred in 16% and fatal cardiac disorders occurred in 10% of patients. Patients with NYHA Class IIIA or Mayo Stage IIIA disease may be at greater risk. Patients with NYHA Class IIIB or IV disease were not studied. Monitor patients with cardiac involvement of light chain (AL) amyloidosis more frequently for cardiac adverse reactions and administer supportive care as appropriate.

Neutropenia

Daratumumab may increase neutropenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX *FASPRO®* until recovery of neutrophils. In lower body weight patients receiving DARZALEX *FASPRO®*, higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia

Daratumumab may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX *FASPRO*® until recovery of platelets.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX *FASPRO*® can cause fetal harm when administered to a pregnant woman. DARZALEX *FASPRO*® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX *FASPRO*® and for 3 months after the last dose.

The combination of DARZALEX *FASPRO*® with lenalidomide is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide prescribing information on use during pregnancy.

Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted.

Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX *FASPRO*®*.* Type and screen patients prior to starting DARZALEX *FASPRO*®.

Interference with Determination of Complete Response

Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some DARZALEX *FASPRO*®-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

The most common adverse reaction (≥20%) with DARZALEX *FASPRO*® monotherapy is upper respiratory tract infection. The most common adverse reactions with combination therapy (≥20% for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, pyrexia, cough, muscle spasms, back pain, vomiting, upper respiratory tract infection, peripheral sensory neuropathy, constipation, pneumonia, and peripheral edema.

The most common adverse reactions (≥20%) in patients with light chain (AL) amyloidosis who received DARZALEX *FASPRO*® are upper respiratory tract infection, diarrhea, peripheral edema, constipation, fatigue, peripheral sensory neuropathy, nausea, insomnia, dyspnea, and cough.

The most common hematology laboratory abnormalities (≥40%) with DARZALEX *FASPRO*® are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please see full Prescribing Information for DARZALEX *FASPRO*®.

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 and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

[†]Dr. Moreau has served as a paid consultant to Janssen; he has not been paid for any media work.

Kyprolis is a registered trademark of Amgen Inc.

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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 teclistamab and DARZALEX FASPRO®. 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, Janssen Biotech, Inc., 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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