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Janssen Presents Updated Results Evaluating First-in-Class Talquetamab (GPRC5DxCD3 Bispecific Antibody) in Heavily Pretreated Patients with Multiple Myeloma

Updated results of weekly and biweekly dosing of talquetamab monotherapy and initial results in combination with daratumumab presented in oral presentations at the ASH 2021 Annual Meeting

ATLANTA, Ga., December 11, 2021– The Janssen Pharmaceutical Companies of Johnson & Johnson announced today updated results from the MonumenTAL-1 Phase 1 first-in-human dose-escalation study of talquetamab (NCT03399799). Talquetamab is the only investigational off-the-shelf T cell redirecting bispecific antibody in clinical development targeting both GPRC5D, a novel multiple myeloma target, and CD3 on T cells.[1] Results from the study show that no new safety signals were observed with longer follow-up.[1] Heavily pretreated patients with multiple myeloma treated with talquetamab at the recommended subcutaneous (SC) Phase 2 doses (RP2D) administered weekly (QW) and every two weeks (Q2W) achieved high overall responses that deepened over time.[1] These data were featured during the American Society of Hematology (ASH) 2021 Annual Meeting as an oral presentation (Abstract #158).[1]

No new safety signals were identified with longer follow-up of either dose cohort.[1] The most common adverse events (AEs) at the SC 405 µg/kg QW dose were cytokine release syndrome (CRS – 77 percent; three percent grade 3), neutropenia (67 percent; 60 percent grade 3/4) and dysgeusia (60 percent).[1] Dysgeusia was generally mild with few dose adjustments required. The most common AEs at the SC 800 µg/kg Q2W dose were CRS (72 percent; all grade 1/2), neutropenia (44 percent; 36 percent grade 3/4), and dry mouth (40 percent; all grade 1/2).[1] Cytopenias were mostly confined to step-up doses and cycles one and two and were reversible, including neutropenias which generally resolved within a week. Infections occurred in 33 percent of patients and there was a low rate of high-grade infections (five percent grade 3/4).[1] Skin-related and nail disorder AEs occurred in 75 percent of patients, most commonly exfoliation (37 percent at SC 405 µg/kg QW; 36 percent at 800 µg/kg Q2W, all grade 1/2), which did not lead to treatment modification.[1] Injection site reactions occurred in 16 percent of patients and were all grade 1/2.[1]

Pre-treatment medications (including glucocorticoid, antihistamine, and antipyretic treatments) were only required at the step-up and first full doses, and no steroid treatment was required after the first full dose.

"New treatment options are needed for patients with multiple myeloma," said Amita Krishnan, M.D., Chief, Division of Multiple Myeloma, Department of Hematology and Hematopoietic Cell Transplantation, City of Hope Comprehensive Cancer Center, Duarte, California, and principal study investigator.[†] "The continued observation of a tolerable safety profile and durable responses seen in these updated data suggest that in both doses, talquetamab may offer a new treatment option for heavily pretreated patients."

With a median follow-up of nine months (range 0.9-17.1), 70 percent (21/30) of response-evaluable patients treated with the SC 405 µg/kg QW dose achieved a response, 53 percent achieved a very good partial response (VGPR) or better, 13 percent achieved a complete response (CR) or better, and 10 percent achieved a stringent complete response (sCR).[1] With a median follow-up of 4.8 months (range 0.4-11.1), 67 percent (14/21) of response-evaluable patients treated with the SC 800 µg/kg Q2W dose achieved a response, 52

percent achieved a VGPR or better, 19 percent achieved a CR or better, and 10 percent achieved an sCR.[1] The median duration of response (DOR) was not reached for either dose.[1]

Among response-evaluable patients who were triple-class refractory, a response was achieved by 65 percent (15/23) of patients treated with the SC 405 µg/kg QW dose and 67 percent (12/18) of patients treated with the SC 800 µg/kg Q2W dose.[1] In patients who were penta-drug refractory, 83 percent (5/6) of patients responded in both dose groups.[1]

"These new data provide important insights into the potential safety, efficacy and tolerability of talquetamab for relapsed and refractory patients," said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Research and Development, Janssen Research & Development, LLC. "We look forward to fully evaluating this novel bispecific antibody as both a monotherapy and in combination immunotherapy regimens."

The primary objectives of the MonumenTAL-1 study were to identify the recommended subcutaneous Phase 2 dose(s) (part 1) and assess the safety and tolerability of talquetamab at the recommended dose (part 2).[1] As of September 2021, 102 patients with multiple myeloma who had relapsed or become refractory or intolerant to established therapies have received SC talquetamab in the study.[1] For part 2, 30 patients received the weekly RP2D of SC 405 µg/kg QW dosing schedule with step-up doses; 100 percent were triple-class exposed, 80 percent were penta-drug exposed, 77 percent were triple-class refractory, 20 percent were penta-drug refractory and 27 percent had prior B-cell maturation antigen (BCMA)-directed therapy.[1] Twenty-five patients received the SC RP2D of 800 µg/kg Q2W; 92 percent were triple-class exposed; 68 percent were penta-drug exposed; 76 percent were triple-class refractory, 24 percent were penta-drug refractory, and 16 percent had prior BCMA-directed therapy.[1]

Data from the Phase 2 TRiMM-2 Study Evaluating Talquetamab in Combination with DARZALEX *FASPRO*® (Abstract #161)

Additional data for talquetamab will be highlighted in an oral presentation at ASH on Saturday, December 11 (Abstract #161).[2] The Phase 1b TRIMM-2 investigational study (NCT04108195) evaluated talquetamab 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. Results suggest that the combination is tolerable in patients with relapsed or refractory multiple myeloma who had received a median of six prior lines of therapy (range 2-18), with a safety profile comparable to each agent as a monotherapy at each of three doses evaluated in the study.[2]

Patients received step-up doses of talquetamab of SC 400 µg/kg QW (n=9); SC 400 µg/kg Q2W (n=5); or SC 800 µg/kg Q2W (n=15), in combination with DARZALEX *FASPRO*® at the approved dosing schedule.[2] At a median follow up of 4.2 months, 86 percent (6/7) of response-evaluable patients treated with the SC 400 µg/kg QW achieved a response, and 80 percent (4/5) of patients treated with the SC 400 µg/kg Q2W dose achieved a response. At the SC 800 µg/kg Q2W dose of talquetamab 78 percent (7/9) of patients achieved a response.[2]

The safety profile of the combination appeared consistent with each agent as a monotherapy.[2] At all doses, the most common AE was cytokine release syndrome (CRS), observed in 55 percent (16/29) of patients.[2] All CRS events were grade 1/2 and all but one event occurred with step-up doses of talquetamab.[2] CRS resolved in all patients, and no patients discontinued treatment due to CRS.[2] Other AEs included dysgeusia (48 percent; all grade 1/2) and dry mouth (35 percent; all grade 1/2).[2] Skin-related and nail disorders were reported in 65 percent of patients (all grade 1/2); the most commonly reported skin or nail event was skin exfoliation (28 percent, all grade 1/2).[2] One patient experienced immune effector cell-associated neurotoxicity syndrome (ICANS), including one grade 3 event and one grade 1 event, both of which resolved yet resulted in discontinuation of talquetamab.[2]

The primary objectives of the TRiMM-2 study were to identify the Phase 2 dose (RP2D) for each component of the treatment combination (Part One); characterize the safety of the treatment combination at the RP2D (Part 2); and assess antitumor activity, pharmacokinetics and pharmacodynamics for the combination treatment (Part 3).[2] Patients in the study (n=29) all had multiple myeloma and had received a minimum three prior lines of therapy or were double refractory to a proteasome inhibitor (PI) and an

immunomodulatory agent; patients who had been exposed or refractory to an anti-CD38 therapy more than ninety days prior to the start of the trial were also included, as well as those refractory to anti-CD38 therapy.[2]

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.[3] CD3 is involved in activating T-cells, and GPRC5D is highly expressed on multiple myeloma cells.[4,5] 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.**Error! Bookmark not defined.**

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). In January 2021, talquetamab was granted PRIority MEdicines (PRIME) designation by the European Commission.

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.[6,7] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow.[7,8] 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. 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.[8]

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 www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal. Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

[†]Dr. Krishnan has served as a consultant to Janssen; she 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 talquetamab and DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj). 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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