News Release

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Janssen Presents Updated Data at EHA for Teclistamab in Patients with Relapsed or Refractory Multiple Myeloma

Data show a combination of teclistamab (BCMAxCD3 bispecific antibody) plus DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) improved clinical efficacy in heavily pretreated patients with relapsed or refractory multiple myeloma

June 10, 2022 (VIENNA) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced updated efficacy and safety results from the teclistamab cohort of the Phase 1b TriMM-2 study (NCT04108195). Teclistamab, an investigational, off-the-shelf, T-cell redirecting bispecific antibody targeting B-cell maturation antigen (BCMA) is being studied in combination with DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) in patients with relapsed or refractory multiple myeloma (RRMM) who have received three or more prior lines of therapy.[1] Patients in the study, including a high proportion with prior anti-CD38 exposure, achieved encouraging overall response rates (ORR) with this combination treatment.[1] These data will be presented at the 2022 European Hematology Association (EHA) Annual Congress as an oral presentation on Sunday, June 12 (Abstract S188).[1]

At a median follow-up of 8.6 months (range, 0.3-19.6), 76.5 percent (39/51) of response-evaluable patients enrolled in the study achieved a response, including 36 patients (70.6

percent) who achieved a very good partial response (VGPR) or better.[1] In patients with prior anti-CD38 exposure, an ORR of 73.7 percent was achieved.[1] The median time to first confirmed response was one month, and responses remained durable and deepened over time.[1] At the analysis cutoff, 66.7 percent of patients who achieved a response (26/39) were alive and continuing on therapy.[1]

"Responders to the combination of teclistamab plus subcutaneous daratumumab included patients with prior exposure to BCMA or anti-CD38 targeted agents, which is encouraging," said Paula Rodríguez-Otero†, M.D., Ph.D., Department of Hematology, Clínica Universidad de Navarra, Pamplona, Spain and principal study investigator. "These data also suggest this steroid-sparing regimen may lead to a clinically efficacious regimen in highly refractory patients."

The open-label, multicenter, multicohort Phase 1b TriMM-2 study is investigating the safety and efficacy of teclistamab in combination with DARZALEX *FASPRO*® for patients with RRMM. Enrolled patients received a median of five prior lines of therapy, 58.5 percent were triple-class refractory, 30.8 percent were penta-drug refractory, and 63.1 percent were refractory to anti-CD38 treatment.[1] Eighty percent of patients were refractory to their last line of therapy.[1]

As of April 6, 2022, 65 patients received daratumumab 1800mg at the approved schedule plus teclistamab 1.5mg/kg weekly (QW) or 3mg/kg every other week (Q2W) subcutaneously.[1] Pre-medications, including steroids, were limited to the two step-up doses and the first full dose of teclistamab.[1] Treatment with the combination regimen were tolerable and no unexpected or overlapping toxicities were observed.[1] The most common adverse events were cytokine release syndrome (CRS) (67.7 percent, all Grade 1 or 2); neutropenia (49.2 percent, 41.5 percent Grade 3 or 4); and anemia (41.5 percent, 27.7 percent Grade 3 or 4).[1] One patient (2 percent) had Grade 1 immune effector cell–associated neurotoxicity syndrome (ICANS) which fully resolved.[1] Infections were experienced by 67.7 percent of patients (27.7 percent Grade 3 or 4).[1] Four patients died from adverse events, all unrelated to teclistamab or daratumumab treatment.[1]

"These data suggest the potential of a fully immune-based regimen for patients with heavily pretreated multiple myeloma," said Yusri Elsayed, M.D., M.HSc., Ph.D., Vice President, Disease Area Leader, Hematologic Malignancies, Janssen Research & Development, LLC.

"We are committed to the ongoing development of this combination and other treatments for patients who remain in need of new options."

Pharmacodynamic analyses demonstrate that the combination upregulates CD38+/CD8+ T-cells and proinflammatory cytokines, suggesting the potential for synergistic activity.[4] Additional studies are needed to fully understand the potential clinical benefit of this biological activity.

The efficacy and pharmacodynamic profile of teclistamab in combination with DARZALEX *FASPRO*® in patients refractory to anti-CD38 therapy suggest that higher response rates may be observed in patients with anti-CD38 naïve or sensitive disease who are enrolling in the MajesTEC-3 study (NCT05083169).[1] The ongoing Phase 3 MajesTEC-3 study compares the efficacy of the teclistamab-daratumumab combination with daratumumab subcutaneously (SC) in combination with pomalidomide and dexamethasone (DPd) or daratumumab SC in combination with bortezomib and dexamethasone (DVd).[2] Patients in the trial must have received one to three prior lines of therapy including a proteasome inhibitor (PI) and lenalidomide; patients who have received only one prior line of therapy must be refractory to lenalidomide.[2] Patients who have progressed on or within 60 days of the last dose of lenalidomide given as maintenance therapy are also included.[2]

About Teclistamab

Teclistamab is an investigational, fully humanized, T-cell redirecting, IgG4 bispecific antibody targeting both BCMA (B-cell maturation antigen) and CD3, the T-cell receptor. BCMA is expressed at high levels on multiple myeloma cells.[3,4,5,6,7] Teclistamab redirects CD3-positive T-cells to BCMA-expressing myeloma cells to induce killing of tumor cells.[6]

Teclistamab is currently being evaluated in several monotherapy and combination studies. In 2020, the European Commission and the U.S. Food and Drug Administration (FDA) both 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 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 based on preliminary clinical evidence that demonstrates the drug may have substantial improvement in at least one clinically significant endpoint over available therapy.[9] In December 2021, Janssen submitted a Biologics License Application (BLA) to the FDA seeking approval of teclistamab for the treatment of patients with relapsed or refractory multiple myeloma; a marketing authorization application (MAA) was submitted to the EMA for teclistamab approval in January 2022.

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.

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, tachycardia, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. 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, pruritus, chills, vomiting, nausea, hypotension, and blurred vision.

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.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with daratumumab-containing products. If ocular symptoms occur, interrupt DARZALEX *FASPRO*® and seek immediate ophthalmologic evaluation prior to restarting DARZALEX *FASPRO*®*.*

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 AL Amyloidosis

Serious or fatal cardiac adverse reactions occurred in patients with AL amyloidosis who received DARZALEX *FASPRO*® in combination with bortezomib, cyclophosphamide, and dexamethasone. Serious cardiac disorders occurred in 16% of patients, 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 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, thalidomide, or pomalidomide is contraindicated in pregnant women because lenalidomide, thalidomide, and pomalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, thalidomide, or pomalidomide 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 immunoglobulin G (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

In multiple myeloma, 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, headache, pyrexia, cough, muscle spasms, back pain, vomiting, hypertension, upper respiratory tract infection, peripheral sensory neuropathy, constipation, pneumonia, and peripheral edema.

The most common adverse reactions (≥20%) in patients with AL amyloidosis 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 Multiple Myeloma

Multiple myeloma is an incurable blood cancer that affects some white blood cells called plasma cells, which are found in the bone marrow.[10] When damaged, these plasma cells rapidly spread and replace normal cells in the bone marrow with tumors. In 2020, an estimated 176,000 people worldwide were diagnosed with multiple myeloma.[11] In 2022, it is estimated that more than 34,000 people will be diagnosed with multiple myeloma, and more than 12,000 people will die from the disease in the U.S.[12] While some people diagnosed 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]

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, & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at @JanssenGlobal. Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

[†]Dr. Paula Rodríguez-Otero has served as a paid 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 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 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 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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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