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Janssen Submits Application to U.S. FDA Seeking Approval of DARZALEX® (daratumumab) Combination Therapy for Patients with Newly Diagnosed Multiple Myeloma Who Are Transplant Ineligible

Application supported by the Phase 3 MAIA study being reviewed under the FDA Real-Time Oncology Review pilot program

RARITAN, NJ, March 12, 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the submission of a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) seeking approval of DARZALEX® (daratumumab) in combination with lenalidomide and dexamethasone (Rd) for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).

The sBLA, based upon data from the Phase 3 MAIA (MMY3008) clinical study, is being reviewed by the FDA under the Real-Time Oncology Review (RTOR) pilot program, which for certain applications allows the FDA to review data before the applicant formally submits the

complete application. It aims to explore a more efficient review process to help ensure treatments are available as soon as possible for patients. Selection into the RTOR pilot program does not guarantee or influence approvability of the supplemental application.

"We are pleased to complete the latest DARZALEX submission based upon the Phase 3 MAIA study, which evaluated the efficacy and safety of this anti-CD38 monoclonal antibody as a combination regimen for newly diagnosed patients with multiple myeloma who are transplant ineligible," said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Vice President, Hematologic Malignancies Disease Area Leader, Janssen Research & Development, LLC. "We look forward to closely collaborating with the Agency throughout the expedited Real-Time Oncology Review process in support of this newly diagnosed, transplant ineligible multiple myeloma patient population for whom a combination treatment regimen with DARZALEX may be useful."

Data from the Phase 3 MAIA study were presented at the 2018 American Society of Hematology (ASH) Annual Meeting and featured in the Late-Breaking Abstract session. The study found that at a median follow-up of 28 months, DARZALEX-Rd reduced the risk of disease progression or death by 44 percent in patients with newly diagnosed multiple myeloma who are transplant ineligible compared to treatment with Rd alone (Hazard Ratio [HR] = 0.56; 95 percent confidence interval [CI]: 0.43-0.73; $p<0.0001$).[1] The median progression-free survival for DARZALEX-Rd has not yet been reached, compared to 31.9 months for patients who received Rd alone.[1] The addition of DARZALEX resulted in deeper responses compared to Rd alone, including increased rates of complete response or better (48 percent vs. 25 percent).[1] An improved overall response rate was also demonstrated (93 percent vs. 81 percent).[1]

The most common Grade 3/4 treatment-emergent adverse events for DARZALEX-Rd (≥10 percent) included neutropenia (50 percent), lymphopenia (15 percent), pneumonia (14 percent) and anemia (12 percent).[1] Infusion-related reactions occurred in 41 percent of patients, three percent of which were Grade 3/4.[1] The safety profile of DARZALEX was consistent with that of previous studies.[1]

About the Real-Time Oncology Review Program

The RTOR pilot program aims to explore a more efficient review process to ensure safe and effective treatments become available to patients earlier while maintaining the quality of

review. Applications are subject to the usual benefit-risk evaluation by FDA scientists. The RTOR pilot program is specific to the U.S. regulatory pathway.

About the MAIA Trial[1]

The randomized, open-label, multicenter, Phase 3 study included 737 newly diagnosed patients with multiple myeloma ineligible for high-dose chemotherapy and ASCT aged 45 – 90 years old (median age of 73). Patients were randomized to receive either DARZALEX-Rd or Rd alone in 28-day Cycles. In the DARZALEX-Rd treatment arm, patients received DARZALEX 16 milligrams per kilogram (mg/kg) IV weekly for Cycles 1 – 2, every two weeks for Cycles 3 – 6 and every 4 weeks for Cycle 7 and thereafter. Patients in the DARZALEX-Rd and Rd treatment arm received 25 mg of lenalidomide on Days 1 – 21 of each 28-day Cycle, and dexamethasone at 40 mg once a week for each Cycle. Patients in both treatment arms continued until disease progression or unacceptable toxicity.

About DARZALEX® (daratumumab)

DARZALEX® (daratumumab), the first CD38-directed antibody approved anywhere in the world, is the only CD38-directed antibody approved to treat multiple myeloma.[2] CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[3] DARZALEX binds to CD38 and inhibits tumor cell growth causing myeloma cell death.[2] DARZALEX may also have an effect on normal cells.[2] DARZALEX is being evaluated in a comprehensive clinical development program across a range of treatment settings in multiple myeloma, such as in frontline and relapsed settings.[4,5,6,7,8,9,10,11] Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant hematologic diseases in which CD38 is expressed, such as smoldering myeloma.[12,13]

In the U.S., DARZALEX received initial FDA approval in November 2015 as a monotherapy for patients with multiple myeloma 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.[14] DARZALEX received additional approvals in November 2016 in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.[15] In June 2017, DARZALEX received approval in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies, including lenalidomide

and a PI.[16] Most recently, in May 2018, DARZALEX received approval in combination with bortezomib, melphalan and prednisone for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for ASCT, making it the first monoclonal antibody approved for newly diagnosed patients with this disease.[17]

In August 2012, Janssen Biotech, Inc. entered into a global license and development agreement with Genmab A/S, which granted Janssen an exclusive license to develop, manufacture and commercialize DARZALEX.[18] For the full U.S. Prescribing Information, please visit www.DARZALEX.com.

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.[19,20] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow.[19,20] In 2019, it is estimated that 32,110 people will be diagnosed, and 12,960 will die from the disease, in the U.S.[21] While some patients with multiple myeloma have no symptoms, most patients are diagnosed due to symptoms, which can include bone fracture or pain, low red blood counts, tiredness, high calcium levels, kidney problems or infections.[22]

IMPORTANT SAFETY INFORMATION[2]

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (e.g., anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion Reactions – DARZALEX® can cause severe and/or serious infusion reactions, including anaphylactic reactions. In clinical trials, approximately half of all patients experienced an infusion reaction. Most infusion reactions occurred during the first infusion and were grade 1-2. Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing an infusion. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, laryngeal edema and pulmonary edema. Signs and symptoms may include respiratory symptoms, such

as nasal congestion, cough, throat irritation, as well as chills, vomiting and nausea. Less common symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, and hypotension.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt infusion for reactions of any severity and institute medical management as needed. Permanently discontinue therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

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 infusion. 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®. Type and screen patients prior to starting DARZALEX®.

Neutropenia – DARZALEX® 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. DARZALEX® dose delay may be required to allow recovery of neutrophils. No dose reduction of DARZALEX® is recommended. Consider supportive care with growth factors.

Thrombocytopenia – DARZALEX® may increase thrombocytopenia induced by

background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. DARZALEX® dose delay may be required to allow recovery of platelets. No dose reduction of DARZALEX® is recommended. Consider supportive care with transfusions.

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 patients with IgG kappa myeloma protein.

Adverse Reactions – The most frequently reported adverse reactions (incidence ≥20%) in clinical trials were: infusion reactions, neutropenia, thrombocytopenia, fatigue, nausea, diarrhea, constipation, vomiting, muscle spasms, arthralgia, back pain, pyrexia, chills, dizziness, insomnia, cough, dyspnea, peripheral edema, peripheral sensory neuropathy and upper respiratory tract infection.

In patients who received DARZALEX® in combination with bortezomib, melphalan, and prednisone (DVMP), the most frequently reported adverse reactions (incidence ≥20%) were: upper respiratory tract infection (48%), infusion reactions (28%), and peripheral edema (21%). Serious adverse reactions (≥2% compared to the VMP arm) were pneumonia (11%), upper respiratory tract infection (5%), and pulmonary edema (2%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were lymphopenia (58%), neutropenia (44%), and thrombocytopenia (38%).

In patients who received DARZALEX® in combination with lenalidomide and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were: upper respiratory tract infection (65%), infusion reactions (48%), diarrhea (43%), fatigue (35%), cough (30%), muscle spasms (26%), nausea (24%), dyspnea (21%) and pyrexia (20%). The overall incidence of serious adverse reactions was 49%. Serious adverse reactions (≥2% compared to Rd) were pneumonia (12%), upper respiratory tract infection (7%), influenza (3%), and pyrexia (3%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were neutropenia (53%) and lymphopenia (52%).

In patients who received DARZALEX® in combination with bortezomib and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were: peripheral sensory neuropathy (47%), infusion reactions (45%), upper respiratory tract infection (44%), diarrhea (32%), cough (27%), peripheral edema (22%), and dyspnea (21%). The overall incidence of serious adverse reactions was 42%. Serious adverse reactions (≥2% compared to Vd) were upper respiratory tract infection (5%), diarrhea (2%) and atrial fibrillation (2%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were lymphopenia (48%) and thrombocytopenia (47%).

In patients who received DARZALEX® in combination with pomalidomide and dexamethasone, the most frequent adverse reactions (>20%) were fatigue (50%), infusion reactions (50%), upper respiratory tract infection (50%), cough (43%), diarrhea (38%), constipation (33%), dyspnea (33%), nausea (30%), muscle spasms (26%), back pain (25%), pyrexia (25%), insomnia (23%), arthralgia (22%), dizziness (21%), and vomiting (21%). The overall incidence of serious adverse reactions was 49%. Serious adverse reactions reported in ≥5% patients included pneumonia (7%). Treatment-emergent hematology Grade 3-4 laboratory abnormalities ≥20% were anemia (30%), neutropenia (82%), and lymphopenia (71%).

In patients who received DARZALEX® as monotherapy, the most frequently reported adverse reactions (incidence ≥20%) were: infusion reactions (48%), fatigue (39%), nausea (27%), back pain (23%), pyrexia (21%), cough (21%), and upper respiratory tract infection (20%). The overall incidence of serious adverse reactions was 33%. The most frequent serious adverse reactions were pneumonia (6%), general physical health deterioration (3%), and pyrexia (3%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were lymphopenia (40%) and neutropenia (20%).

DRUG INTERACTIONS

Effect of Other Drugs on Daratumumab: The coadministration of lenalidomide, pomalidomide or bortezomib with DARZALEX® did not affect the pharmacokinetics of daratumumab.

Effect of Daratumumab on Other Drugs: The coadministration of DARZALEX® with bortezomib or pomalidomide did not affect the pharmacokinetics of bortezomib or pomalidomide.

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/JanssenGlobal. Janssen Research & Development, LLC and Janssen Biotech, Inc. are members of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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 development of DARZALEX. 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, 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 December 30, 2018, 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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[1] Clinicaltrials.gov. Study Comparing Daratumumab, Lenalidomide, and Dexamethasone with Lenalidomide and Dexamethasone in Participants with Previously Untreated Multiple Myeloma. https://clinicaltrials.gov/ct2/show/NCT02252172. Accessed March 2019.
[2] DARZALEX Prescribing Information, June 2018.
[3] Fedele G et al. CD38 Ligation in Peripheral Blood Mononuclear Cells of Myeloma Patients Induces Release of Protumorigenic IL-6 and Impaired Secretion of IFNγ Cytokines and Proliferation. Mediators Inflamm. 2013;564687.
[4] Janssen Research & Development, LLC. A Study Comparing Daratumumab, Lenalidomide, and Dexamethasone With Lenalidomide and Dexamethasone in Relapsed or Refractory Multiple Myeloma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02076009?term=mmy3003&rank=1 Identifier: NCT02136134.
[5] Janssen Research & Development, LLC. Addition of Daratumumab to Combination of Bortezomib and Dexamethasone in Participants With Relapsed or Refractory Multiple Myeloma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02136134?term=mmy3004&rank=1 Identifier: NCT02076009.
[6] Janssen Research & Development, LLC. A Study to Evaluate Daratumumab in Transplant Eligible Participants With Previously Untreated Multiple Myeloma (Cassiopeia). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02541383?term=mmy3006&rank=2 NLM Identifier: NCT02541383.
[7] Janssen Research & Development, LLC. A Study of Combination of Daratumumab and Velcade (Bortezomib) Melphalan-Prednisone (DVMP) Compared to Velcade Melphalan-Prednisone (VMP) in Participants With Previously Untreated Multiple Myeloma In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02195479?term=mmy3007&rank=1 Identifier: NCT02195479.
[8] Janssen Research & Development, LLC. Study Comparing Daratumumab, Lenalidomide, and Dexamethasone With Lenalidomide and Dexamethasone in Participants With Previously Untreated Multiple Myeloma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02252172?term=mmy3008&rank=1 Identifier: NCT02252172.
[9] Janssen Research & Development, LLC. A Study of VELCADE (Bortezomib) Melphalan-Prednisone (VMP) Compared to Daratumumab in Combination With VMP (D-VMP), in Participants With Previously Untreated Multiple Myeloma Who Are Ineligible for High-Dose Therapy (Asia Pacific Region). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT03217812?term=MMY3011&rank=1 Identifier: NCT03217812.
[10] European Myeloma Network. Compare Progression Free Survival Btw Daratumumab/Pomalidomide/Dexamethasone vs Pomalidomide/Dexamethasone (EMN14). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24] Available at: https://clinicaltrials.gov/ct2/show/NCT03180736?term=MMY3013&rank=2 Identifier: NCT03180736
[11] Amgen. Study of Carfilzomib, Daratumumab and Dexamethasone for Patients With Relapsed and/or Refractory Multiple Myeloma. (CANDOR). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24] Available at:

https://clinicaltrials.gov/ct2/show/NCT03158688?term=NCT03158688&rank=1 Identifier: NCT03158688.
[12] Janssen Research & Development, LLC. A Study to Evaluate 3 Dose Schedules of Daratumumab in Participants With Smoldering Multiple Myeloma In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 March 19]. Available at: https://clinicaltrials.gov/ct2/show/NCT02316106?term=smm2001&rank=1 Identifier: NCT02316106.
[13] Janssen Research & Development, LLC. An Efficacy and Safety Proof of Concept Study of Daratumumab in Relapsed/Refractory Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, and Follicular Lymphoma In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 March 19]. Available at: https://clinicaltrials.gov/ct2/show/NCT02413489?term=lym2001&rank=1 Identifier: NCT02413489
[14] Janssen Biotech, Inc. "DARZALEX® (daratumumab) Approved by U.S. FDA: First Human Anti-CD38 Monoclonal Antibody Available for the Treatment of Multiple Myeloma." Issued November 16, 2015.
[15] Janssen Biotech, Inc. "DARZALEX® (daratumumab) Approved by U.S. FDA in Combination with Two Standard of Care Regimens for the Treatment of Patients with Multiple Myeloma Who Have Received At Least One Prior Therapy." Issued November 21, 2016.
[16] Janssen Biotech, Inc. "DARZALEX® (daratumumab) Approved by the U.S. FDA in Combination with Pomalidomide and Dexamethasone for Patients with Multiple Myeloma Who Have Received At Least Two Prior Therapies." Issued June 16, 2017.
[17] Janssen Pharmaceutical Companies of Johnson & Johnson. "Janssen Announces DARZALEX® (daratumumab) U.S. FDA Approval for Newly Diagnosed Patients with Multiple Myeloma who are Transplant Ineligible." Issued May 7, 2018.
[18] Janssen Biotech, Inc. "Janssen Biotech Announces Global License and Development Agreement for Investigational Anti-Cancer Agent Daratumumab." Issued August 30, 2012.
[19] Kumar, SK et al. Leukemia. 2012 Jan; 26(1):149-57.
[20] American Cancer Society. "What Is Multiple Myeloma?" Available at: http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma. Accessed March 2019.
[21] American Cancer Society. "Key Statistics for Multiple Myeloma." Available at: https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html. Accessed March 2019.
[22] American Cancer Society. "Diagnosing Multiple Myeloma From Test Results." Available at: http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-diagnosis. Accessed March 2019.