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Janssen Submits Application for DARZALEX® (daratumumab) Combination Therapy to U.S. FDA for Newly Diagnosed, Transplant Eligible Patients with Multiple Myeloma

First DARZALEX combination treatment regimen being pursued in the frontline setting for transplant eligible patients with multiple myeloma

RARITAN, NJ, March 26, 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 bortezomib, thalidomide and dexamethasone (VTd) for newly diagnosed patients with multiple myeloma who are eligible for autologous stem cell transplant (ASCT). The Phase 3 CASSIOPEIA (MMY3006) clinical study, which supports the sBLA submission, met its primary endpoint – the proportion of patients that achieved stringent Complete Response (sCR) after induction and consolidation therapy.[1]

"This submission marks an important step in the pursuit of potential treatments for newly diagnosed patients living with multiple myeloma, as DARZALEX has the potential to improve clinical outcomes in combination with a standard regimen," 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 working closely with the FDA during review of the submission with the goal of bringing a new treatment option to newly diagnosed patients who are transplant eligible."

About the CASSIOPEIA Trial[1]

The randomized, open-label, multicenter, Phase 3 study is sponsored by the French Intergroupe Francophone du Myelome (IFM) in collaboration with the Dutch-Belgian Cooperative Trial Group for Hematology Oncology (HOVON) and Janssen Research & Development, LLC. The study included 1,085 newly diagnosed patients with previously untreated symptomatic multiple myeloma who were eligible for high-dose chemotherapy and stem cell transplant. In the first part of the study, patients were randomized to receive induction treatment with VTd alone or in combination with DARZALEX, high-dose therapy and ASCT, and consolidation therapy with VTd alone or in combination with DARZALEX. The primary endpoint in this part of the study is the proportion of patients who achieve a sCR. In the second part of the study, which is ongoing, patients who achieved a partial response or better in part one will undergo a second randomization to receive maintenance treatment with DARZALEX 16 mg/kg every eight weeks for up to two years or be observed with no further treatment. The primary endpoint in this part of the study is progression-free survival.

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 (eg, 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.

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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 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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