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**Final Analysis of Phase 2 GRIFFIN Study Presented for DARZALEX®
(daratumumab)-based Investigational Quadruplet Regimen in Patients with Newly
Diagnosed, Transplant-Eligible Multiple Myeloma**

Data featured in plenary session at the 19th International Myeloma Society Annual Meeting

LOS ANGELES, August 27, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the final results from the randomized Phase 2 GRIFFIN study evaluating the investigational use of DARZALEX® (daratumumab) in combination with lenalidomide (Revlimid®), bortezomib (VELCADE®) and dexamethasone (DARZALEX®-RVd), followed by maintenance therapy with DARZALEX®-lenalidomide (R), compared to RVd followed by maintenance therapy with R alone, in patients with newly diagnosed, transplant-eligible multiple myeloma. Data were presented in the plenary session at the 19th International Myeloma Society (IMS) Annual Meeting.

In the primary analysis (median follow-up of 13.5 months), the GRIFFIN study met its primary endpoint, resulting in a higher stringent complete response (sCR) rate for DARZALEX®-RVd compared with RVd alone by the end of post-autologous stem cell transplant (ASCT) consolidation therapy (42.4 percent vs. 32 percent; 1-sided $P=0.0680$) meeting the prespecified 1-sided alpha of 0.1. At IMS, the predefined final analysis for GRIFFIN (median follow-up of 49.6 months), which occurred after all patients had completed at least one year of follow-up after end of study therapy or withdrew, showed that longer progression-free survival (PFS) was observed in patients who received DARZALEX®-RVd/DARZALEX®-R compared to those who received RVd/R (hazard ratio = 0.45; 95 percent confidence interval, 0.21-0.95; $P=0.0324$).¹ Higher minimal residual disease (MRD) negativity rates were observed for DARZALEX®-RVd vs. RVd (64 percent vs. 30 percent). No new safety concerns were observed with longer-term follow-up.

“The final analysis of the GRIFFIN trial highlights the potential benefit of adding daratumumab to RVd for the treatment of newly diagnosed, transplant-eligible patients,” said Douglas W. Sborov[†], M.D., M.S., Director of the Multiple Myeloma Program at the Huntsman Cancer Institute at the University of Utah and GRIFFIN study investigator. “We are constantly investigating the role of new regimens and combinations to improve outcomes in our patients and GRIFFIN is another important step forward in this research.”

Final Analysis from GRIFFIN

After two years of maintenance therapy, the MRD negativity rate continued to favor DARZALEX®-RVd versus RVd (64 percent vs. 30 percent; $P<0.0001$). Additionally, 44 percent of patients who received DARZALEX®-RVd achieved sustained MRD negativity lasting 12 months or more, compared to 14 percent of patients in the RVd arm. Treatment with DARZALEX®-RVd also resulted in higher sCR rates at all time points in the study, with the highest rates occurring following two years of maintenance therapy (67 percent vs. 48 percent; $P=0.0079$, respectively). CR or better rate was 83 percent in the DARZALEX®-RVd arm vs. 60 percent in the RVd arm ($P=0.005$).

At the conclusion of the final analysis, after a median follow-up of 49.6 months, a 55 percent reduction in the risk of disease progression or death was observed in patients in the DARZALEX®-RVd arm; an estimated 48-month PFS rate of 87.2 percent was observed in the DARZALEX®-RVd arm, compared to 70 percent in the RVd arm. Median PFS was not reached in either treatment arm. In addition, after extended follow-up, no new safety concerns were observed.

“The Phase 2 GRIFFIN study showed important results with the investigational DARZALEX® quadruplet regimen in the treatment of newly diagnosed, transplant-eligible multiple myeloma,” said Imran Khan, M.D., Ph.D., U.S. Vice President, Medical Affairs, Hematology at Janssen Scientific Affairs, LLC. “The evaluation of this treatment regimen will continue as part of the registrational, Phase 3 PERSEUS study. These studies represent our ongoing focus in multiple myeloma and our commitment to advance research and new therapeutic combinations for patients at each stage of their treatment journey.”

About the GRIFFIN Study

The Phase 2 GRIFFIN ([NCT02874742](https://clinicaltrials.gov/ct2/show/study/NCT02874742)) study evaluated the investigational regimen of DARZALEX® in combination with RVD and enrolled and treated more than 200 adults ages 18-70 years with newly diagnosed multiple myeloma who were eligible for ASCT.

In the safety run-in cohort, 16 patients received 25 mg of lenalidomide orally on days 1-14; 1.3 mg/m² of bortezomib subcutaneously on days 1, 4, 8 and 11; and 20 mg of dexamethasone on days 1, 2, 8, 9, 15 and 16, and every 21 days during the induction and consolidation phases (cycles 1-6). DARZALEX® 16 mg/kg IV was given on days 1, 8 and 15 of cycles 1-4 and on day 1 of cycles 5-6.

During the maintenance phase (cycles 7-32), patients received 10 mg daily of lenalidomide (15 mg beginning at cycle 10 if tolerated) on days 1-21 every 28 days and DARZALEX® 16 mg/kg IV every 56 days; this was amended to every 28 days based upon emerging clinical pharmacokinetic data demonstrating improved target saturation with every-4-week maintenance dosing. Maintenance therapy with lenalidomide could be continued beyond cycle 32, per local standard of care.

In the subsequent randomized Phase 2 portion of the study, 207 patients were randomized to treatment with RVD induction and consolidation, ASCT, and maintenance therapy with lenalidomide; or DARZALEX®-RVD, ASCT, and maintenance therapy with DARZALEX® and lenalidomide.

Janssen’s clinical development program continues to evaluate the potential of DARZALEX®-containing quadruplet regimens in improving clinical outcomes for patients.

About DARZALEX®

Janssen is committed to exploring the potential of DARZALEX® (daratumumab) for patients with multiple myeloma across the spectrum of the disease. DARZALEX® has been approved

in eight indications, three of which are in the frontline setting, including newly diagnosed patients who are transplant eligible and ineligible.²

In [August 2012](#), Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize daratumumab. DARZALEX® has become a backbone therapy in the treatment of multiple myeloma, having been used in the treatment of more than 300,000 patients worldwide and more than 68,000 patients in the U.S. alone since its U.S. FDA approval in 2015.³ DARZALEX® is the first CD38-directed antibody approved globally to treat multiple myeloma.⁵

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.⁴ DARZALEX® binds to CD38 and inhibits tumor cell growth, causing myeloma cell death.⁴ DARZALEX® may also have an effect on normal cells.⁴ Data across eight Phase 3 clinical trials, in both the frontline and relapsed settings, have shown that DARZALEX®-based regimens resulted in significant improvement in PFS and/or OS.^{5,6,7,8,9,10,11,12}

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.^{2,3} When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow. In 2022, it is estimated that more than 34,000 people will be diagnosed and close to 12,000 will die from the disease in the U.S.¹³ 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 cell counts, tiredness, high calcium levels, kidney problems or infections.⁴

INDICATIONS

DARZALEX® (daratumumab) is indicated for the treatment of adult patients with multiple myeloma:

- 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, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant

- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- 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
- In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- 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

IMPORTANT SAFETY INFORMATION

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-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension and blurred vision.

When DARZALEX[®] dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX[®], the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX[®] following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX[®] infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX[®] 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-related 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.

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 DARZALEX[®] infusion. If ocular symptoms occur, interrupt DARZALEX[®] infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX[®].

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 is 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 and Thrombocytopenia

DARZALEX® may increase neutropenia and thrombocytopenia 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® until recovery of neutrophils or for recovery of platelets.

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 patients with IgG kappa myeloma protein.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX® can cause fetal harm when administered to a pregnant woman. DARZALEX® 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® and for 3 months after the last dose.

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

ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence $\geq 20\%$) were upper respiratory infection, neutropenia, infusion-related reactions, thrombocytopenia, diarrhea, constipation, anemia, peripheral sensory neuropathy, fatigue, peripheral edema, nausea, cough, pyrexia, dyspnea, and asthenia. The most common hematologic laboratory abnormalities ($\geq 40\%$) with DARZALEX® are neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Please [click here](#) to see the full Prescribing Information.

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.

[†]Douglas W. Sborov, M.D., M.S., has served as a consultant to Janssen; he has not been paid for any media work.

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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, 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 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.

¹ Sborov, D et al. Daratumumab (DARA) Plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients (Pts) With Transplant-eligible Newly Diagnosed Multiple Myeloma (NDMM): Final Analysis of GRIFFIN after ≥ 1y follow up. To be presented at the International Myeloma Society 2022 Annual Meeting

² DARZALEX® Prescribing Information, March 2021.

³ Data on File. Janssen Biotech, Inc.

⁴ Moreau P et al. Phase 3 randomized study of daratumumab (DARA) + bortezomib/thalidomide/dexamethasone (D-VTd) vs VTd in transplant-eligible (TE) newly diagnosed multiple myeloma (NDMM): CASSIOPEIA Part 1 results. Presented at Annual Meeting of the American Society of Clinical Oncology (ASCO), Chicago, IL, USA, 31 May – 4 June 2019: abstract 8003.

⁵ 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=mmv3003&rank=1>. Identifier: NCT02076009.

⁶ 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=mmv3004&rank=1>. Identifier: NCT02136134.

⁷ 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=mmv3006>. Identifier: NCT02541383.

⁸ 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=mmv3007&rank=1>. Identifier: NCT02195479.

⁹ 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=mmv3008&rank=1>. Identifier: NCT02252172.

¹⁰ 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=MMV3011&rank=1>. Identifier: NCT03217812.

¹¹ 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=MMV3013&rank=2>. Identifier: NCT03180736.

¹² 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.

¹³ American Cancer Society. "Key Statistics About Multiple Myeloma." Available at: <https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html#:~:text=The%20American%20Cancer%20Society's%20estimates,men%20and%205%2C570%20in%20women>. Accessed August 2022.