Media contacts:
Satu Glawe
+49 172-294-6264

Virginia Chess
+1 609-240-9332

Investor Relations:
Jessica Moore
+1 732-524-2955

U.S. Medical Inquiries:
+1 800-526-7736

New Clinical and Real-World Data Support Use of DARZALEX® (daratumumab) in Patients with Newly Diagnosed Multiple Myeloma

Investigational DARZALEX® quadruple combination regimen shows responses in newly diagnosed, transplant-eligible patients in randomized Phase 2 GRIFFIN study

Real-world evidence analysis examines the impact of frontline versus second-line treatment with DARZALEX®-based combinations in transplant-ineligible patients

ATLANTA, Ga., December 11, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today new analyses illustrating responses that first-line treatment with DARZALEX® (daratumumab)-based regimens may be able to achieve, including a potential survival benefit for DARZALEX® in combination with

lenalidomide and dexamethasone (Rd). Updated data from the randomized Phase 2 GRIFFIN study in transplant-eligible patients and real-world evidence in transplant-ineligible patients were presented at the American Society of Hematology (ASH) 2021 Annual Meeting. Data from the GRIFFIN study will also be featured in the Highlights of ASH program.

Updated Phase 2 GRIFFIN data of investigational DARZALEX® quadruple regimen for newly diagnosed transplant-eligible patients

Updated results from the GRIFFIN study, now with a median follow-up of 38.6 months, were presented in an oral session (Abstract #79). The data show improved outcomes with the addition of DARZALEX® to bortezomib (VELCADE®), lenalidomide (Revlimid®) and dexamethasone (VRd), followed by DARZALEX® plus lenalidomide (R) maintenance therapy, in transplant-eligible patients. Key findings included:

- The rate of stringent complete response (sCR) favored DARZALEX®-VRd compared to VRd alone (66 percent vs. 47.4 percent; p=0.0096).[1]
- Minimal residual disease (MRD) negativity rates at a threshold of 10^{-5} remained significantly higher in patients treated with DARZALEX®-VRd vs. VRd alone (64.4 percent vs. 30.1 percent; p<0.0001).[1]
- At 36 months, the progression-free survival (PFS) rate trended toward favoring DARZALEX®-VRd compared to VRd alone (88.9 percent vs. 81.2 percent).
    - At the median follow-up of 38.6 months, median progression-free survival (mPFS) had not been reached in either arm.[1]
- No new safety concerns were observed with longer-term follow up.[1]

"These updated findings from the GRIFFIN study are promising when adding daratumumab to VRd in the treatment of newly diagnosed, transplant-eligible multiple myeloma," said Jacob Laubach, M.D., M.P.P.†, Clinical Director of the Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute and GRIFFIN study investigator.

Additional analyses of DARZALEX®-based regimens for the treatment of transplant-ineligible newly diagnosed multiple myeloma

Research shows that 50 percent of transplant-ineligible patients will not receive a second line of therapy.[2] An oral presentation at ASH 2021 highlighted clinical sequencing scenarios in patients with newly diagnosed transplant-ineligible multiple myeloma, utilizing data from the Phase 3 MAIA trial, including attrition rates, and real-world evidence from the Flatiron Health electronic health record-derived de-identified database* (Abstract 118). Researchers explored survival outcomes based on clinical sequencing scenarios using DARZALEX® first in combination with Rd, compared to when VELCADE® was administered first in combination with Rd. Results from this analysis suggest a potential for a survival benefit when patients received DARZALEX® in first-line treatment versus saving it for later. Future research is required to generate clinical data to confirm these results.

A second presentation of real-world evidence data provided additional insights on sequencing, based on results from a retrospective, observational cohort study evaluating patients from the Flatiron database who received first-line DARZALEX®-Rd (Abstract #1979). The analysis indicated that the real-world patient population was similar to that of the MAIA study population, with an early trend of PFS similar to that observed in the MAIA trial.

A post-hoc analysis of the Phase 3 MAIA study, focusing on patients with renal impairment, was highlighted in a poster presentation (Abstract #1646). Research shows that approximately 20 to 50 percent of patients with multiple myeloma have baseline renal impairment that can impact their choice of treatment and efficacy. The exploratory analyses presented at ASH showed that PFS and overall survival (OS) benefits were observed in these patients who were treated with DARZALEX®-Rd compared to Rd alone, regardless of the lenalidomide starting dose. OS data from the MAIA study were recently published in *The Lancet Oncology*.

"The clinical data presented at ASH support DARZALEX as a foundational therapy for patients with newly diagnosed multiple myeloma in transplant-ineligible populations," said Imran Khan, M.D., Ph.D., U.S. Vice President, Medical Affairs, Hematology, Janssen Scientific Affairs, LLC. "Real-world evidence about efficacy, safety and

adherence is becoming increasingly important for clinicians in optimizing treatment approaches for patients with multiple myeloma. We will continue to advance research that can provide important insights about DARZALEX as part of a standard of care regimen in the frontline setting."

About the GRIFFIN Study

The Phase 2 GRIFFIN (NCT02874742) study evaluated the investigational regimen of DARZALEX® in combination with VRd and enrolled and treated more than 200 adults ages 18-70 years with newly diagnosed multiple myeloma who were eligible for high-dose therapy/autologous stem cell transplant (ASCT).

In the safety run-in cohort, patients received 25 mg of lenalidomide orally on days 1-14; 1.3 mg/m^2 of bortezomib subcutaneously on days 1, 4, 8 and 11; and 20 mg of dexamethasone on days 1, 2, 8, 9, 15 and 16, 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 may be continued beyond cycle 32 in both arms, per local standard of care.

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

Janssen continues to invest in a clinical development program evaluating the potential of DARZALEX®-containing quadruple regimens in improving clinical outcomes for patients.

About the MAIA Study

The randomized, open-label, multicenter Phase 3 MAIA study (NCT02252172) included 737 newly diagnosed patients with multiple myeloma ineligible for high-dose chemotherapy and ASCT, aged 45-90 years (median age of 73).[1] Patients were randomized to receive either DARZALEX®-Rd (D-Rd) or Rd alone in 28-day cycles. In the D-Rd arm, patients received DARZALEX® 16 mg/kg IV weekly for cycles 1-2, every two weeks for cycles 3-6 and every 4 weeks for cycle 7 and thereafter.[1] Patients in both treatment arms received 25 mg of lenalidomide on days 1-21 of each 28-day cycle, and dexamethasone at 40 mg once a week. Patients in both treatment arms continued until disease progression or unacceptable toxicity.[1]

Earlier results from the MAIA study supported the U.S. Food and Drug Administration (FDA) approval of DARZALEX® in combination with Rd, marking the first approval of a CD-38 monoclonal antibody for patients with transplant-ineligible newly diagnosed multiple myeloma. These data were also published in *The New England Journal of Medicine* in 2019.

Modeling and Real-World Data Limitations

Modeling and real-world data have the potential to supplement randomized controlled trial data by providing additional information about how a medicine performs across all available Phase 2 and 3 clinical trials and in routine clinical practice. There are limitations, however, and these data cannot be used as stand-alone evidence to validate the efficacy or safety of a treatment.

*The Flatiron Health database is a longitudinal database comprising de-identified, patient-level structured and unstructured data curated via technology-enabled abstraction.

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.[3]

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 227,000 patients worldwide and more than 68,000 patients in the U.S. alone since its U.S. FDA approval in 2015.[4] 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.[5] 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.[6,7,8,9,10,11,12,13]

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 2021, it is estimated that more than 34,000 people will be diagnosed and close to 12,500 will die from the disease in the U.S.[2,4] 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]

DARZALEX® 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
- 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

IMPORTANT SAFETY INFORMATION

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-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, 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.

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, i.e., 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.

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 ≥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 (≥40%) with DARZALEX® are: neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

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.*

[†]Jacob Laubach, M.D., M.P.P., 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 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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