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News Release

Media contact:
Noah Reymond
Mobile : +31 621 38 5718
Email : Nreymond@ITS.JNJ.com

Investor Relations:
Jessica Moore
Mobile: +41 79 395 4823
Email: Jmoore29@its.jnj.com

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

Investigational daratumumab quadruple combination regimen shows responses in newly diagnosed, transplant-eligible patients with multiple myeloma in randomised Phase 2 GRIFFIN study[1]

Real-world evidence analysis examines the impact of frontline versus second-line treatment with daratumumab-based combinations in transplant-ineligible patients[2]

BEERSE, BELGIUM, 11 December 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 daratumumab in combination with lenalidomide and dexamethasone (Rd).[1,2] Updated data from the randomised 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 programme.

"Despite treatment advances, multiple myeloma remains a complex, currently incurable blood cancer. The latest clinical trial data and real-world evidence presented for daratumumab at ASH shines a light on the potential of daratumumab-based combinations and sequencing approaches in the first-line, to tackle this complexity and improve patient outcomes," said Edmond Chan MBChB M.D. (Res), EMEA Therapeutic Area Lead Haematology, Janssen-Cilag Limited. "At Janssen, we are committed to developing transformative treatment regimens that address individual patient needs and offer physicians options which they have not had before, as we work towards our longer-term goal of curing multiple myeloma."

Updated Phase 2 GRIFFIN data of investigational daratumumab quadruple regimen for newly diagnosed transplant-eligible patients[1]

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 daratumumab to bortezomib (VELCADE®), lenalidomide (Revlimid®) and dexamethasone (VRd), followed by daratumumab plus lenalidomide (R) maintenance therapy, in transplant-eligible patients.[1] Key findings included:

- The rate of stringent complete response (sCR) favoured daratumumab-VRd compared to VRd alone (66 percent versus 47.4 percent; p=0.0096).[1,3]
- Minimal residual disease (MRD) negativity rates at a threshold of 10^{-5} remained significantly higher in patients treated with daratumumab-VRd versus VRd alone (64.4 percent versus 30.1 percent; p<0.0001).[1,3]
- Whilst this study was not powered for progression-free survival (PFS), at 36 months, the PFS rate trended toward favouring daratumumab-VRd compared to VRd alone (88.9 percent versus 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 daratumumab-based regimens for the treatment of transplant-ineligible newly diagnosed multiple myeloma[2]

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, utilising data from the Phase 3 MAIA study, including attrition rates, and real-world evidence from the Flatiron Health electronic health record-derived de-identified database* (Abstract 118).[2] Researchers explored survival outcomes based on clinical sequencing scenarios using daratumumab first in combination with Rd, compared to when bortezomib was administered first in combination with Rd.[2] Results from this modelled analysis suggest a potential for a survival benefit when patients received daratumumab in first-line treatment versus saving it for later.[2] 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 daratumumab-Rd (Abstract #1979).[4] 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 study.[4]

A post-hoc analysis of the Phase 3 MAIA study, focusing on patients with renal impairment, was highlighted in a poster presentation (Abstract #1646).[5] 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.[5] The exploratory analyses presented at ASH showed that PFS and overall survival (OS) benefits were observed in these patients who were treated with daratumumab-Rd compared to Rd alone, regardless of the lenalidomide starting dose.[5] OS data from the MAIA study were recently published in *The Lancet Oncology*.

"The clinical data presented at ASH support daratumumab 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 optimising treatment approaches for patients with multiple myeloma. We will continue to advance research that can provide important insights about daratumumab as part of a standard of care regimen in the frontline setting."

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About the GRIFFIN Study[1,6]

The Phase 2 GRIFFIN (NCT02874742) study evaluated the investigational regimen of daratumumab in combination with VRd and enrolled and treated more than 200 adults aged 18–70 years with newly diagnosed multiple myeloma (NDMM) and who were eligible for high-dose therapy/autologous stem cell therapy (ASCT).[6]

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).[1] Daratumumab 16 mg/kg IV was given on days 1, 8 and 15 of Cycles 1–4 and on day 1 of Cycles 5–6.[1]

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 daratumumab 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 four-week maintenance dosing.[1] Maintenance therapy with lenalidomide may be continued beyond Cycle 32 in both arms, per local standard of care.[1]

In the subsequent randomised Phase 2 portion of the study, 207 patients were randomised and received treatment with VRd induction and consolidation, ASCT, and maintenance therapy with lenalidomide; or daratumumab and VRd, ASCT, and maintenance therapy with daratumumab and lenalidomide.[1]

About the MAIA Study[7]

The randomised, open-label, multicentre 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).[7] Patients were randomised to receive either daratumumab-Rd or Rd alone in 28-day cycles. In the daratumumab-Rd arm, patients received daratumumab 16 mg/kg IV weekly for Cycles 1–2, every two weeks for Cycles 3–6 and every four weeks for Cycle 7 and thereafter.[7] 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.[7] Patients in both treatment arms continued until disease progression or unacceptable toxicity.[7]

Earlier results from the MAIA study supported the European Commission (EC) approval of daratumumab in combination with Rd, marking the first approval of a CD38 monoclonal antibody for patients with transplant-ineligible NDMM. These data were also published in *The New England Journal of Medicine* in 2019.

Modelling and Real-World Data Limitations

Modelling and real-world data have the potential to supplement randomised 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 daratumumab

Janssen is committed to exploring the potential of daratumumab for patients with multiple myeloma across the spectrum of the disease. Daratumumab has been approved in eight indications for multiple myeloma, three of which are in the frontline setting, including newly diagnosed patients who are transplant eligible and ineligible.[8]

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialise daratumumab. Since launch, daratumumab has become a foundational therapy in the treatment of multiple myeloma, having been used in the treatment of more than 227,000 patients worldwide.[9] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma. Daratumumab subcutaneous (SC) formulation is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[10]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[8] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[8] Daratumumab may also have an effect on normal cells.[8] Data across eight Phase 3 clinical trials, in both the frontline and relapsed settings, have shown that daratumumab-based regimens resulted in significant improvement in PFS and/or OS.[11,12,13,14,15,16,17,18]

For further information on daratumumab, please see the Summary of Product Characteristics at:
https://www.ema.europa.eu/en/documents/product-information/darzalex-epar-product-information_en.pdf

About Multiple Myeloma

Multiple myeloma is currently an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[19] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow.[19] In Europe, more than 50,900 people were diagnosed with multiple myeloma in 2020, and more than 32,500 patients died.[20] 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.[21]

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/EMEA. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag Limited and Janssen Scientific Affairs, LLC. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

[†]Jacob Laubach has served as a consultant to Janssen; he has not been paid for any media work.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding daratumumab. 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 Pharmaceutica NV, Janssen-Cilag Limited, Janssen Scientific Affairs, LLC., *Janssen Biotech, Inc., 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 behaviour 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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