Media Enquiries:
Noah Reymond
Mobile: +31 62138 5718
Email: NReymond@ITS.JNJ.com

Investor Relations:
Christopher DelOrefice
Phone: +1 732-524-2955

Lesley Fishman
Phone: +1 732-524-3922

Janssen Seeks Expanded Use of DARZALEX®▼ (daratumumab) Combination Therapy for Patients with Newly Diagnosed Multiple Myeloma Who Are Transplant Ineligible

Application supported by the Phase 3 MAIA study for daratumumab in combination with lenalidomide and dexamethasone for the treatment of patients newly diagnosed with multiple myeloma who are ineligible for autologous stem cell transplant

BEERSE, BELGIUM, 22 March 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a Type II variation application to the European Medicines Agency (EMA) for DARZALEX®▼ (daratumumab) in combination with lenalidomide and dexamethasone (Rd) for the treatment of patients newly diagnosed with multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).

"Today's submission brings us one step closer to our goal of improving treatment outcomes for people newly diagnosed with multiple myeloma," said José Antonio Burón Vidal, VP Medical Affairs, Europe, Middle East and Africa (EMEA), Janssen-Cilag Limited. "We are incredibly grateful to the patients and investigators who participated in the MAIA clinical trial programme and look forward to working closely with the regulatory authorities to secure approval of this new combination."

The submission is supported by data from the Phase 3 MAIA (MMY3008) study, which were presented at the 60th Annual Meeting of the American Society of Hematology.[1] The study showed that at a median follow-up of 28 months, daratumumab-Rd significantly 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 (PFS) for daratumumab-Rd has not yet been reached, compared to 31.9 months for patients who received Rd alone.[1] The addition of daratumumab resulted in deeper responses compared to Rd alone, including increased rates of complete response (CR) or better (48 percent vs. 25 percent) and improved rates of very good partial response (VGPR) or better (79 percent vs. 53 percent).[1] Within the study, patient health, functional capacity, symptoms, psychosocial well-being, and life satisfaction were evaluated through measures to assess change in health-related quality of life by the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and Euro Quality of Life (EQ-5D-5L) Health State Profile Utility Score.[2]

The most common Grade 3/4 treatment-emergent adverse events (TEAEs) for daratumumab-Rd (≥10 percent) included neutropenia (50 percent), lymphopenia (15 percent), pneumonia (14 percent) and anaemia (12 percent).[1] Infusion-related reactions (IRRs) occurred in 41 percent of patients receiving daratumumab-Rd, 3 percent of which were Grade 3/4.[1] Incidence of invasive second primary malignancy was 3 percent in the daratumumab-Rd arm compared to 4 percent with Rd alone.[1] TEAEs with an outcome of death were 7 percent in the daratumumab-Rd arm compared to 6 percent in the Rd arm.[1] The safety profile of daratumumab was consistent with that of previous studies.[1,3,4,5,6,7]

Daratumumab-Rd is being reviewed by the U.S. Food and Drug Administration (FDA) under the Real-Time Oncology Review (RTOR) pilot programme.

In Europe, daratumumab is indicated:[8]

- in combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant
- as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy
- in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

#ENDS#

About the MAIA Trial[2]

The randomised, open-label, multicentre 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 years). Patients were randomised to receive either daratumumab-Rd or Rd alone in 28-day Cycles. In the daratumumab-Rd treatment arm, patients received daratumumab 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. Patients in the daratumumab-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 daratumumab

Daratumumab is a first-in-class biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[9,10] Daratumumab is believed to induce tumour cell death through multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), as well as through apoptosis, in which a series of molecular steps in a cell lead to its death.[11] A subset of myeloid derived suppressor cells (CD38+ MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by daratumumab.[11] Daratumumab is being evaluated in a comprehensive clinical development programme across a range of treatment settings in multiple myeloma, such as in frontline and relapsed settings.[2,12,13,14,15,16,17,18] Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant haematologic diseases in which CD38 is expressed, such as smouldering myeloma.[19,20] For more information, please see www.clinicaltrials.gov.

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

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive licence to develop, manufacture and commercialise daratumumab.[21]

About Multiple Myeloma

Multiple myeloma (MM) is an incurable blood cancer that starts in the bone marrow and is characterised by an excessive proliferation of plasma cells.[22] In Europe, more than 48,200 people were diagnosed with MM in 2018, and more than 30,800 patients died.[23] Up to half of newly diagnosed patients do not reach five-year survival,[24] and almost 29% of patients with MM will die within one year of diagnosis.[25]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[26] Refractory MM is when a patient's disease progresses within 60 days of their last therapy.[27,28] Relapsed cancer is when the disease has returned after a period of initial, partial or complete remission.[29] While some patients with MM have no symptoms at all, most patients are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[30] Patients who relapse after treatment with standard therapies, including proteasome inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[31]

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 Biotech, Inc., Janssen-Cilag International NV, and Janssen-Cilag Limited are part 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 a recommendation to broaden the existing marketing authorisation for 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 materialise, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, Janssen-Cilag Limited, Janssen Biotech, Inc., any of the Janssen Pharmaceutical Companies of Johnson & Johnson 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 December 30, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," in the company's most recently filed Quarterly Report on Form 10-Q and in 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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