FOR EU MEDICAL AND TRADE MEDIA ONLY

Media Enquiries:
Noah Reymond
Mobile: +31 621 38 5718
Email: NReymond@its.jnj.com

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

Lesley Fishman
Phone: +1 732-524-3922

Janssen Receives EU Marketing Authorisation for Darzalex®▼(daratumumab) in Combination with Lenalidomide and Dexamethasone for Patients with Newly Diagnosed Multiple Myeloma Who Are Transplant Ineligible

- *Combination regimen reduces the risk of disease progression or death by 44 percent in newly diagnosed patients who are transplant ineligible*[1]
- *Since launch, daratumumab has been used to treat more than 100,000 patients worldwide*[2]

BEERSE, BELGIUM, 19 November 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the European Commission (EC) has granted marketing authorisation for Darzalex® (daratumumab) in combination with lenalidomide and dexamethasone (DRd) for the treatment of newly diagnosed multiple myeloma patients who are ineligible for autologous stem cell transplant (ASCT). The approval was based on results from the Phase 3 MAIA (MMY3008) study, published in *The New England Journal of Medicine*[3] earlier this year and presented at the American Society of Hematology (ASH) Annual Meeting in 2018.

"Despite recent therapeutic advances, relapse of multiple myeloma is considered to be almost inevitable, becoming more challenging to treat following each relapse. This makes it even more important that we maximise our best response upfront to extend the first remission," said Professor Thierry Facon, M.D., Service des Maladies du Sang, Hôspital Claude Huriez, Lille, France, and principal investigator of the MAIA study. "This marks an important approval, especially for transplant ineligible patients, a more vulnerable population, for whom outcomes are generally poorer when compared to those who are transplant eligible."

The 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).[1] Daratumumab in combination with 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] At median follow-up of 28.0 months the median progression-free survival (PFS) for daratumumab-Rd had 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] Daratumumab-Rd induced a >3-fold higher rate of minimal residual disease (MRD) negativity compared to those who received Rd alone (24 percent vs. 7 percent).[1]

"Every year over 48,000 people in Europe are diagnosed with multiple myeloma, which is considered to be incurable. Older patients who are ineligible for transplant have a limited range of frontline therapeutic options available, so we are pleased that with today's approval of daratumumab-Rd, these patients now have a new frontline option available to them," said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag.

Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC., commented: "It's gratifying to see that through our research and development efforts, daratumumab has helped over 100,000 patients globally. With today's approval and the continued development of daratumumab, we hope to bring this innovative therapy to many more patients in the future."

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, only 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]

In Europe, daratumumab is indicated:[4]

- 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,
- 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,
- as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor (PI) and an immunomodulatory agent, and who have demonstrated disease progression on the last therapy.

#**ENDS**#

About the MAIA (NCT02252172) Trial[5]

In this open-label and multicentre Phase 3 study 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. The primary endpoint was Progression-Free Survival, defined as the time from date of randomisation to either progressive disease, or death, whichever occurred first. 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[6] biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[7] 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.[4] A subset of myeloid derived suppressor cells (CD38+ MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by daratumumab.[4] Since launch, it is estimated that 100,000 patients have been treated with daratumumab worldwide.[2] 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.[5,8,9,10,11,12,13,14] 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.[15,16] For more information, please see https://www.clinicaltrials.gov/.

For further information on daratumumab, please see the Summary of Product Characteristics at https://www.ema.europa.eu/en/medicines/human/EPAR/darzalex.

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.[17]

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that starts in the bone marrow and is characterised by an excessive proliferation of plasma cells.[18] In Europe, more than 48,200 people were diagnosed with MM in 2018, and more than 30,800 patients died.[19] Almost 60 percent of patients with MM do not survive more than five years after diagnosis.[20]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[21] Refractory MM is when a patient's disease progresses within 60 days of their last therapy.[22,23] Relapsed cancer is when the disease has returned after a period of initial, partial or complete remission.[24] 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.[25] Patients who relapse after treatment with standard therapies, including proteasome inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[26]

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-Cilag, Janssen Biotech, Inc. and Janssen Research & Development, LLC 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 the benefits of daratumumab for the treatment of patients with multiple myeloma. 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 of the 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 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. Neither the Janssen Pharmaceutical Companies of Johnson & Johnson nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

###

References

[1] Facon T, Kumar SJ, Plesner T, et al. Phase 3 Randomized Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patients with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant (MAIA). Presented at the 60th Annual Meeting and Exposition of the American Society of Hematology, San Diego, CA, USA, 1-4 December 2018: Oral presentation.

[2] Janssen Data on file. RF-82203. New patient starts: launch to date. October 2019.

[3] Facon T, Kumar S, Plesner T, et al. Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med.*;380:2104-2115.

[4] European Medicines Agency. DARZALEX summary of product characteristics, August 2019. Available at: https://www.ema.europa.eu/documents/product-information/darzalex-epar-product-information_en.pdf Last accessed November 2019.

[5] ClinicalTrials.gov. Study Comparing Daratumumab, Lenalidomide, and Dexamethasone With Lenalidomide and Dexamethasone in Participants With Previously Untreated Multiple Myeloma. NCT02252172. Available at: https://clinicaltrials.gov/ct2/show/NCT02252172 Last accessed November 2019.

[6] Sanchez L, Wang Y, Siegel DS, Wang ML. Daratumumab: a first-in-class CD38 monoclonal antibody for the treatment of multiple myeloma. *J Hematol Oncol*. 2016;9:51.

[7] Fedele G, di Girolamo M, Recine U, et al. CD38 ligation in peripheral blood mononuclear cells of myeloma patients induces release of protumorigenic IL-6 and impaired secretion of IFNgamma cytokines and proliferation. *Mediat Inflamm*. 2013;2013:564687.

[8] ClinicalTrials.gov. A study to evaluate daratumumab in transplant eligible participants with previously untreated multiple myeloma (Cassiopeia). NCT02541383. Available at: https://clinicaltrials.gov/ct2/show/NCT02541383 Last accessed November 2019.

[9] ClinicalTrials.gov. A study comparing daratumumab, lenalidomide, and dexamethasone with lenalidomide and dexamethasone in relapsed or refractory multiple myeloma. NCT02076009. Available at: https://clinicaltrials.gov/ct2/show/NCT02076009 Last accessed November 2019.
[10] ClinicalTrials.gov. Addition of daratumumab to combination of bortezomib and dexamethasone in participants with relapsed or refractory multiple myeloma. NCT02136134. Available at: https://clinicaltrials.gov/ct2/show/NCT02136134 Last accessed November 2019.
[11] ClinicalTrials.gov. 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. NCT02195479. Available at: https://clinicaltrials.gov/ct2/show/NCT02195479 Last accessed November 2019.
[12] ClinicalTrials.gov. 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). NCT03217812. Available at: https://clinicaltrials.gov/ct2/show/NCT03217812 Last accessed November 2019.
[13] ClinicalTrials.gov. Comparison of pomalidomide and dexamethasone with or without daratumumab in subjects with relapsed or refractory multiple myeloma previously treated with lenalidomide and a proteasome inhibitor daratumumab/pomalidomide/dexamethasone vs pomalidomide/dexamethasone (EMN14). NCT03180736. Available at: https://clinicaltrials.gov/ct2/show/NCT03180736 Last accessed November 2019.
[14] ClinicalTrials.gov. Study of carfilzomib, daratumumab and dexamethasone for patients with relapsed and/or refractory multiple myeloma (CANDOR). NCT03158688. Available at: https://clinicaltrials.gov/ct2/show/NCT03158688 Last accessed November 2019.
[15] ClinicalTrials.gov. A study to evaluate 3 dose schedules of daratumumab in participants with smoldering multiple myeloma. NCT02316106. Available at: https://clinicaltrials.gov/ct2/show/NCT02316106 Last accessed November 2019.
[16] ClinicalTrials.gov. An efficacy and safety proof of concept study of daratumumab in relapsed/refractory mantle cell lymphoma, diffuse large B-cell lymphoma, and follicular lymphoma. NCT02413489. Available at: https://clinicaltrials.gov/ct2/show/NCT02413489 Last accessed November 2019.
[17] Johnson & Johnson. Janssen Biotech announces global license and development agreement for investigational anti-cancer agent daratumumab. Press release August 30, 2012. Available at: https://www.jnj.com/media-center/press-releases/janssen-biotech-announces-global-license-and-development-agreement-for-investigational-anti-cancer-agent-daratumumab Last accessed November 2019.
[18] American Society of Clinical Oncology. Multiple myeloma: introduction. Available at: https://www.cancer.net/cancer-types/multiple-myeloma/introduction Last accessed November 2019.
[19] GLOBOCAN 2018. Cancer Today Population Factsheets: Europe Region. Available at: https://gco.iarc.fr/today/data/factsheets/populations/908-europe-fact-sheets.pdf Last accessed November 2019.
[20] De Angelis R, Minicozzi P, Sant M, et al. Survival variations by country and age for lymphoid and myeloid malignancies in Europe 2000-2007: results of EUROCARE-5 population-based study. *Eur J Cancer.* 2015;51:2254-68.
[21] Abdi J, Chen G, Chang H, et al. Drug resistance in multiple myeloma: latest findings and new concepts on molecular mechanisms. *Oncotarget*. 2013;4:2186–207.
[22] National Cancer Institute. NCI dictionary of cancer terms: refractory. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms?CdrID=350245 Last accessed November 2019.
[23] Richardson P, Mitsiades C, Schlossman R, et al. The treatment of relapsed and refractory multiple myeloma. *Hematology Am Soc Hematol Educ Program*. 2007:317-23.
[24] National Cancer Institute. NCI dictionary of cancer terms: relapsed. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms?CdrID=45866 Last accessed November 2019.
[25] American Cancer Society. Multiple myeloma: early detection, diagnosis and staging. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8740.00.pdf Last accessed November 2019.
[26] Kumar SK, Lee JH, Lahuerta JJ, et al. Risk of progression and survival in multiple myeloma relapsing after therapy with IMiDs and bortezomib: a multicenter international myeloma working group study. *Leukemia*. 2012;26:149-57.