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CHMP Grants Positive Opinion for Expanded Use of Darzalex®▼ (daratumumab) in Combination with Bortezomib, Thalidomide and Dexamethasone (VTd) for Patients with Newly Diagnosed Multiple Myeloma Who Are Transplant Eligible

- *If approved by the European Commission, the daratumumab-VTd regimen would represent the first therapeutic option indicated for newly diagnosed patients who are eligible for a stem cell transplant in six years¹*
- *Since launch, daratumumab has been used to treat more than 100,000 patients worldwide²*

BEERSE, BELGIUM, 13 December 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended broadening the existing marketing authorisation for Darzalex®▼ (daratumumab) to include the use of daratumumab in combination with bortezomib, thalidomide and dexamethasone (VTd) for the treatment of adult patients with newly diagnosed patients with multiple myeloma who are eligible for autologous stem cell transplant (ASCT).

The Positive Opinion is supported by data from Part 1 of the Phase 3 CASSIOPEIA ([MMY3006](#)) study, published in *The Lancet*³ in June 2019, and presented at the 2019 American Society of Clinical Oncology (ASCO) Meeting. Additional information about this study can be found at www.ClinicalTrials.gov (NCT02541383).

“Today’s Opinion takes us a step closer to offering the first daratumumab combination regimen to transplant eligible patients, redefining treatment for those people newly diagnosed with multiple myeloma,” said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag. “We are committed to

delivering advances in multiple myeloma care, including providing innovative treatment options that meet the evolving needs of people living with this disease.”

Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology at Janssen Research & Development, LLC., commented: “Our robust clinical development programme continues to demonstrate that daratumumab provides a foundation for the treatment of patients with multiple myeloma across the treatment continuum.”

The CHMP’s Positive Opinion comes after the US Food and Drug Administration’s approval in [September 2019](#). It will now be reviewed by the European Commission, which has the authority to grant marketing authorisation for medicines in the European Economic Area.

#ENDS#

In Europe, daratumumab is indicated:⁴

- in combination with lenalidomide and dexamethasone or 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 and an immunomodulatory agent and who have demonstrated disease progression on the last therapy

About the CASSIOPEIA Trial⁵

The randomised, open-label, multicentre, Phase 3 study is sponsored by the French Intergroupe Francophone du Myelome in collaboration with the Dutch-Belgian Cooperative Trial Group for Hematology Oncology and Janssen Research & Development, LLC. The study included 1,085 newly diagnosed patients with previously untreated, symptomatic multiple myeloma who were eligible for high-dose chemotherapy and stem cell transplant. In the first part of the study, patients were randomised to receive induction treatment with VTd alone or in combination with daratumumab, high-dose therapy and ASCT, and consolidation therapy with VTd alone or in combination with daratumumab. The primary endpoint in this part of the study is the proportion of patients who achieve an sCR 100 days after transplant. In the second part of the study, which is ongoing, patients who achieved a partial response or better in part one will undergo a second randomisation to

receive maintenance treatment with daratumumab 16 mg/kg every eight weeks for up to two years or will be observed with no further treatment. The primary endpoint in this part of the study is progression-free survival (PFS).

About daratumumab

Daratumumab is a first-in-class⁶ 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 (MM) 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 Research & Development, LLC and Janssen Biotech, Inc. 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 Johnson & Johnson. European Commission Approves VELCADE® As A Frontline Induction Therapy Before Stem Cell Transplantation. Press release August 8, 2013. Available at: <https://www.jnj.com/media-center/press-releases/european-commission-approves-velcade-as-a-frontline-induction-therapy-before-stem-cell-transplantation> Last accessed December 2019.
- ² Janssen. Data on file: RF-82203. Daratumumab: New patient starts launch to date. November 2019
- ³ Moreau P, Attal M, Hulin C, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. *Lancet*. 2019;394:29-38.
- ⁴ European Medicines Agency. DARZALEX summary of product characteristics, November 2019. Available at: https://ec.europa.eu/health/documents/community-register/2019/20191119146548/anx_146548_en.pdf Last accessed December 2019.
- ⁵ 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 December 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 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 December 2019.
- ⁹ 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 December 2019.
- ¹⁰ 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 December 2019.
- ¹¹ 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 December 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 December 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 December 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 December 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 December 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 December 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 December 2019.
- ¹⁸ American Society of Clinical Oncology. Multiple myeloma: introduction. Available at: <https://www.cancer.net/cancer-types/multiple-myeloma/introduction> Last accessed December 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 December 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 EURO CARE-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 December 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 December 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 December 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.