

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

Office: +1 732-524-2955

Jennifer McIntyre

Office: +1 732 524 3922

**European Commission Grants Marketing Authorisation for
DARZALEX[®]▼ (daratumumab) Subcutaneous Formulation for all Currently
Approved Daratumumab Intravenous Formulation Indications**

- *New subcutaneous, fixed-dose formulation of daratumumab reduces treatment time from hours to minutes, with comparable efficacy and fewer infusion-related reactions^{1,2}*
- *Daratumumab is now the only approved subcutaneous CD38-directed antibody for the treatment of these multiple myeloma indications in Europe*

BEERSE, BELGIUM, 04 June, 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the European Commission (EC) has granted marketing authorisation for DARZALEX[®]▼ (daratumumab) subcutaneous (SC) formulation for the treatment of adult patients with multiple myeloma (MM). Daratumumab SC is administered as a fixed dose, which significantly reduces treatment time, from hours to approximately three to five minutes, when compared to daratumumab intravenous (IV) formulation.¹ In addition, only the first dose of daratumumab SC needs to be administered in an environment where resuscitation facilities are available. The approval applies to all current daratumumab indications in frontline and relapsed/refractory settings, and

patients currently on daratumumab IV can switch to the SC formulation should they choose to.

Data supporting the approval show that daratumumab SC demonstrated a consistent overall response rate (ORR) and a similar safety profile compared with daratumumab IV in patients with relapsed or refractory MM.¹ In addition, there was a nearly two-thirds reduction in systemic infusion-related reactions (IRRs) for daratumumab SC compared to daratumumab IV (13 percent vs. 35 percent, respectively).¹ The novel SC formulation of daratumumab is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20) [Halozyme's *ENHANZE*[®] drug delivery technology].

“Multiple myeloma is an incurable blood cancer that is often associated with time-intensive treatment regimens, which can be burdensome for patients and physicians. Today’s approval marks important progress for the oncology community as it means daratumumab can now be administered in significantly less time, thereby reducing the time patients need to be in the clinical setting,” said Maria-Victoria Mateos, M.D., Ph.D., COLUMBA primary investigator and Director of the Myeloma Unit at University Hospital of Salamanca-IBSAL, Salamanca, Spain. “Given the current health climate, this is timely and welcome news, particularly for immunocompromised patients.”

“This new formulation was specifically designed as the next step in enhancing the treatment experience with daratumumab, without compromising on safety or efficacy,” said Patrick Laroche, M.D., Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag. “Since its first launch, daratumumab has been used by more than 130,000 patients globally, and Janssen is pleased to expand our offering by making the subcutaneous formulation available for all previously approved indications.”

The approval is supported by data from the Phase 2 PLEIADES ([MMY2040](#)) and Phase 3 COLUMBA ([MMY3012](#)) studies.

In the PLEIADES study, which evaluated the efficacy and safety of daratumumab SC in combination therapies, objective responses were demonstrated in

combination with bortezomib, melphalan, and prednisone (D-VMP) in newly diagnosed transplant ineligible patients.² In addition, objective responses were demonstrated in combination with lenalidomide and dexamethasone (D-Rd) in relapsed or refractory patients who received one prior line of therapy.²

In the COLUMBA study, at a median follow-up of 7.5 months, the ORR was 41 percent for patients taking daratumumab SC as a monotherapy, compared to 37 percent for those taking daratumumab IV as a monotherapy (95 percent confidence interval [CI], 1.11 (0.89-1.37); $P < 0.0001$).³ The ORR was similar across all clinically relevant subgroups, including bodyweight.¹ The ratio of geometric means of C_{trough} for daratumumab SC over daratumumab IV was 108 percent (90 percent CI, 96 percent-122 percent).¹ The progression-free survival was comparable between the daratumumab SC and daratumumab IV (Hazard Ratio [HR] = 0.99; 95 percent CI, 0.78-1.26; $P < 0.9258$).¹ The median duration for each SC injection was five minutes, compared to more than three hours with IV infusions.¹

The most common (>5 percent) Grade 3/4 treatment-emergent adverse events (TEAEs) were thrombocytopenia (14 percent vs. 14 percent), anaemia (13 percent vs. 14 percent) and neutropenia (13 percent vs. 8 percent).³ A lower rate of IRRs was observed in the arm that received daratumumab SC compared to daratumumab IV (13 percent vs. 35 percent, respectively) (Odds Ratio = 0.28; 95 percent CI (0.18-0.44); $P < 0.0001$).³ The primary reasons for treatment discontinuation included progressive disease (43 percent in the SC arm vs. 44 percent in the IV arm) and adverse events (7 percent in the SC arm vs. 8 percent in the IV arm).¹

"Today's approval highlights Janssen's commitment to gaining a better understanding of the evolving needs of people living with multiple myeloma, and to the development of new innovations, combinations, and formulations to best meet those needs," adds Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology at Janssen Research & Development, LLC.

Outside of Europe, Janssen recently received approval from the U.S. Food and Drug Administration for the SC formulation of DARZALEX – known locally as

DARZALEX FASPRO™ (daratumumab and hyaluronidase-fihj) – for the treatment of patients with MM.⁴

#ENDS#

In Europe, daratumumab is indicated:⁵

- 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 bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible 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 COLUMBA Study (MMY3012)^{6,7}

The randomised, open-label, multicentre Phase 3 study included 522 patients with multiple myeloma (MM) who had received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD), or whose disease was refractory to both a PI and an IMiD. In the arm that received daratumumab subcutaneous formulation (SC; n=263), patients (median age of 65) received a fixed dose of daratumumab 1,800 milligrams (mg) co-formulated with recombinant human hyaluronidase (rHuPH20) 2,000 Units per millilitre (U/mL), SC weekly for cycles 1 – 2, every two weeks for cycles 3 – 6, and every four weeks for cycle 7 and thereafter. In the arm that received daratumumab intravenous formulation (IV; n=259), patients (median age of 67) received 16 milligrams per kilogram (mg/kg) weekly for cycles 1 – 2, every two weeks for cycles 3 – 6, and every four weeks for cycle 7 and thereafter. Each cycle was 28 days. Patients in both treatment arms continued until disease progression or

unacceptable toxicity. Co-primary endpoints were overall response rate (ORR; non-inferiority = 60 percent retention of the lower bound [20.8 percent] of the 95 percent confidence interval [CI] of the SIRIUS trial, with relative risk [RR] analysed by Farrington-Manning test) and pre-dose cycle 3, day 1 (C3D1) daratumumab C_{trough} (non-inferiority = lower bound of 90 percent CI for the ratio of the geometric means [GM] ≥ 80 percent).

About the PLEIADES Study (MMY2040)⁸

The non-randomised, open-label, parallel assignment Phase 2 PLEIADES trial included 240 adults either newly diagnosed or with relapsed or refractory multiple myeloma (MM). Patients with newly diagnosed MM were treated with 1,800 mg of daratumumab subcutaneous formulation (SC) in combination with either bortezomib, lenalidomide and dexamethasone (D-VRd) or bortezomib, melphalan and prednisone (D-VMP). Patients with relapsed or refractory disease were treated with 1,800 mg of daratumumab SC plus lenalidomide and dexamethasone (D-Rd). The primary endpoint for the D-VMP and D-Rd cohorts was overall response rate (ORR). The primary endpoint for the D-VRd cohort was very good partial response or better rate. An additional cohort of patients with relapsed and refractory MM treated with daratumumab SC plus carfilzomib and dexamethasone was subsequently added to the study.

About daratumumab

Daratumumab is a first-in-class⁹ biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma (MM) cells, regardless of disease stage.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.⁵ A subset of myeloid derived suppressor cells (CD38+ MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) are decreased by daratumumab-mediated cell lysis.⁵ Since launch, it is estimated that 130,000 patients have been treated with daratumumab worldwide.¹¹ Daratumumab is being evaluated in a comprehensive clinical development programme across a range of treatment settings in MM, such as in frontline and relapsed settings.^{12,13,14,15,16,17,18,19} 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.^{20,21} 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.²²

About Multiple Myeloma (MM)

Multiple myeloma (MM) is an incurable blood cancer that starts in the bone marrow and is characterised by an excessive proliferation of plasma cells.²³ In Europe, more than 48,200 people were diagnosed with MM in 2018, and more than 30,800 patients died.²⁴ Around 50 percent of newly diagnosed patients do not reach five-year survival,^{25,26} and almost 29 percent of patients with multiple myeloma will die within one year of diagnosis.²⁷

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.²⁸ Relapsed and refractory myeloma is defined as disease that is nonresponsive while on salvage therapy, or progresses within 60 days of last therapy in patients who have achieved minimal response (MR) or better at some point previously before then progressing in their disease course.²⁹ While some patients with MM have no symptoms at all, others 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 require new therapies for continued disease control.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-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 and projections of 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 29, 2019, 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.

ENHANZE® is a registered trademark of Halozyyme.

###

References

- ¹ Mateos MV, Nahi H, Legiec W, et al. Efficacy and safety of the randomized, open-label, non-inferiority, phase 3 study of subcutaneous (SC) versus intravenous (IV) daratumumab (DARA) administration in patients (pts) with relapsed or refractory multiple myeloma (RRMM): COLUMBA. *J Clin Oncol*. 2019;37(Suppl.): abstract 8005.
- ² Chari A, San-Miguel J, McCarthy H, et al. Subcutaneous daratumumab plus standard treatment regimens in patients with multiple myeloma across lines of therapy: Pleiades study update. *Blood*. 2019;134(Suppl.1):abstract 3152.
- ³ Mateos MV, Nahi H, Legiec W, et al. Efficacy and safety of the randomized, open-label, non-inferiority, phase 3 study of subcutaneous (SC) versus intravenous (IV) daratumumab (DARA) administration in patients (pts) with relapsed or refractory multiple myeloma (RRMM): COLUMBA. Presented at the Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, USA, 31 May – 4 June 2019.
- ⁴ FDA. FDA approves daratumumab and hyaluronidase-fihj for multiple myeloma. Available at: <https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-daratumumab-and-hyaluronidase-fihj-multiple-myeloma> Last accessed May 2020.
- ⁵ European Medicines Agency. DARZALEX summary of product characteristics. Available at: https://www.ema.europa.eu/documents/product-information/darzalex-epar-productinformation_en.pdf Last accessed May 2020.
- ⁶ Mateos MV, Nahi H, Legiec W, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. *The Lancet Haematology*. 2020;7(5):E370-E380.
- ⁷ ClinicalTrials.gov. A Study of Subcutaneous Versus (vs.) Intravenous Administration of Daratumumab in Participants With Relapsed or Refractory Multiple Myeloma. NCT03277105. Available at: <https://clinicaltrials.gov/ct2/show/NCT03277105> Last accessed May 2020.
- ⁸ ClinicalTrials.gov. A Study to Evaluate Subcutaneous Daratumumab in Combination With Standard Multiple Myeloma Treatment Regimens. NCT03412565. Available at: <https://clinicaltrials.gov/ct2/show/NCT03412565> Last accessed May 2020.
- ⁹ 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.
- ¹⁰ 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 IFN γ cytokines and proliferation. *Mediat Inflamm*. 2013;2013:564687.
- ¹¹ [Data on file]. DARZALEX: New Patient Starts Launch to Date. RF-124148
- ¹² 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 May 2020
- ¹³ 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 May 2020.
- ¹⁴ 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 May 2020.
- ¹⁵ 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 May 2020.
- ¹⁶ 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 May 2020.
- ¹⁷ 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 May 2020.
- ¹⁸ 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 May 2020.
- ¹⁹ 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 May 2020.

-
- ²⁰ 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 May 2020.
- ²¹ 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 May 2020.
- ²² 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 May 2020.
- ²³ American Society of Clinical Oncology. Multiple myeloma: introduction. Available at: <https://www.cancer.net/cancer-types/multiple-myeloma/introduction> Last accessed May 2020.
- ²⁴ GLOBOCAN 2018. Cancer Today Population Factsheets: Europe Region. Available at: <https://qco.iarc.fr/today/data/factsheets/populations/908-europe-fact-sheets.pdf> Last accessed May 2020.
- ²⁵ American Society of Clinical Oncology. Multiple Myeloma: Statistics. Available at: <https://www.cancer.net/cancer-types/multiple-myeloma/statistics> Last accessed May 2020.
- ²⁶ Cancer Research UK. Myeloma statistics. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/myeloma> Last accessed May 2020.
- ²⁷ Costa LJ, Gonsalves WI, Kumar SK. Early mortality in multiple myeloma. *Leukemia*. 2015;29:16168.
- ²⁸ 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.
- ²⁹ Rajkumar SV, Harousseau JL, Durie B, Anderson KC, Dimopoulos M, Kyle R, Blade J, Richardson P, Orlowski R, Siegel D, Jagannath S. Consensus recommendations for the uniform reporting of clinical trials: report of the International Myeloma Workshop Consensus Panel 1. *Blood, The Journal of the American Society of Hematology*. 2011 May 5;117(18):4691-5
- ³⁰ 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: May 2020.
- ³¹ 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.