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DARZALEX®▼ (daratumumab) Subcutaneous (SC) Formulation Becomes the First Approved Treatment for Newly Diagnosed Systemic Light Chain Amyloidosis in Europe and Gains an Additional Approval in Pre-Treated Multiple Myeloma

Approval of daratumumab SC-based regimen in Light Chain (AL) amyloidosis is supported by the Phase 3 ANDROMEDA study, which demonstrated significantly higher haematologic complete response rate vs. commonly used standard-of-care regimen

Daratumumab SC is also now the first subcutaneous anti-CD38 monoclonal antibody approved in combination with pomalidomide and dexamethasone in pre-treated multiple myeloma

Beerse, Belgium, 22 June, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the European Commission (EC) has granted marketing authorisation for the expanded use of DARZALEX®▼ (daratumumab) subcutaneous (SC) formulation in two new indications. The first authorisation of these new indications is for the use of daratumumab SC in combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd) for the treatment of adults with newly diagnosed systemic light chain (AL) amyloidosis. This approval makes this daratumumab-based regimen the first approved therapy for AL amyloidosis in Europe.

The second authorisation is for the use of daratumumab SC in combination with pomalidomide and dexamethasone (D-Pd) for the treatment of adults with multiple myeloma (MM) who have received one prior therapy containing a proteasome inhibitor and lenalidomide and were lenalidomide refractory, or who have received at least two prior therapies that included lenalidomide and a proteasome inhibitor, and have demonstrated disease progression on or after the last therapy.

Both AL amyloidosis and MM are complex, incurable blood disorders. AL amyloidosis is a rare and potentially life-threatening disorder caused by a build-up of amyloid, an insoluble protein, in tissues and organs.[1,2] This eventually causes organ deterioration, most commonly in the heart, kidneys and liver.[3]

Multiple myeloma remains an incurable cancer of the plasma cells found in the bone marrow.[4] While there have been several developments in treatments over the years, the complex nature of the disease means that patients can often become resistant to therapy.[5] Outcomes worsen with each relapse and the need for effective treatment options becomes crucial.[5,6]

"Today's approvals mark significant progress for patients living with these blood disorders, especially for AL amyloidosis where patients have long faced an urgent need for approved treatment options," said Edmond Chan, Senior Director, EMEA Therapeutic Area Lead Hematology, Janssen-Cilag Limited. "The outlook for untreated patients has been poor with an average survival of 12-18 months, and only six months for those with severely impaired heart function. Our goal is to change these statistics and offer new hope to patients facing an AL amyloidosis diagnosis."

The EC approval for the AL amyloidosis indication is based on positive results from the Phase 3 ANDROMEDA study, recently presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting and at the 26th European Haematology Association (EHA) Congress.[7,8] The study evaluated D-VCd compared with VCd alone, a common treatment regimen used in adult patients with newly diagnosed AL amyloidosis. Patients receiving treatment with daratumumab experienced a significantly higher haematologic complete response rate (haemCR) compared to patients receiving VCd alone (59 percent vs. 19 percent; $p<0.0001$).[7] Furthermore, at 20.3 months median follow up, more patients achieved a very good partial response or better (≥VGPR) with D-VCd than VCd (79 percent vs 50 percent).[7] Overall, D-VCd had a safety profile consistent with that previously observed for each of the agents alone.[7]

"AL amyloidosis is a rare haematological disorder and can be incredibly challenging to diagnose as symptoms are often subtle and can mimic other conditions. This challenge is further compounded by limited treatment options," said Efstathios Kastritis*, M.D., Professor of Clinical Therapeutics at the National and Kapodistrian University of Athens School of Medicine, Athens, Greece and ANDROMEDA study investigator. "The approval of daratumumab is therefore welcome news for patients and the medical community as the addition of daratumumab to VCd, which has until now been the

standard-of-care regimen for treating AL amyloidosis, has been shown to induce deep responses in patients, not only inducing remission at a significantly greater rate than VCd alone, but also significantly improving cardiac and renal responses and delaying major organ deterioration."

"At Janssen, our goal is to deliver transformative innovations to patients with complex blood disorders," said Jessica Vermeulen, M.D., Ph.D., Vice President Clinical R&D, Late Stage Development, Hematology, Janssen Biologics B.V. "We are focused on the continued research and development of daratumumab for patients who are in need of additional treatment options, and we look forward to realising the impact daratumumab will have in these new indications."

The EC approval for daratumumab SC in combination with Pd in the treatment of pre-treated MM is based on positive findings from the Phase 3 APOLLO study recently published in *The Lancet Oncology*. An updated analysis of the study, featuring health-related quality of life data, was also presented at the American Society of Clinical Oncology (ASCO) Annual Meeting and the 26th European Hematology Association (EHA) Congress.

The APOLLO study met its primary endpoint of improved progression-free survival (PFS), demonstrating that D-Pd significantly reduced the risk of progression or death by 37 percent, compared to Pd alone (hazard ratio, 0.63; 95 percent confidence interval [CI], 0.47-0.85; *P*=0.0018).[9] The median PFS for the D-Pd arm vs. Pd arm was 12.4 vs. 6.9 months, respectively.[9] Study findings additionally showed the rate of overall response to be significantly higher in D-Pd compared to Pd alone (69 percent vs 46 percent), as well as rates of complete response or better (25 percent vs 4 percent) and very good partial response or better (51 percent vs 20 percent).[9] Additionally, more patients treated with D-Pd showed a negative status for minimal residual disease than patients receiving Pd alone (9 percent vs 2 percent).[9] Furthermore, D-Pd demonstrated a consistent safety profile with the known profiles of daratumumab SC or Pd alone.[9]

#ENDS#

About the ANDROMEDA Study[7]

ANDROMEDA (NCT03201965) is an ongoing Phase 3, randomised, open-label study investigating the safety and efficacy of daratumumab SC in combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd), compared to VCd alone, in the treatment of patients with newly diagnosed light chain (AL) amyloidosis. The study includes 388 patients with newly diagnosed AL amyloidosis with measurable haematologic disease and

one or more organs affected. The primary endpoint is overall complete haematologic response rate by intent-to-treat (ITT). Secondary endpoints include major organ deterioration, progression free survival, major organ deterioration event free survival, organ response rate, overall survival, and time to haematologic response, among others.[7]

About the APOLLO Study[10]

APOLLO (NCT03180736) is an ongoing multicentre, Phase 3, randomised, open-label study comparing daratumumab SC, pomalidomide and low-dose dexamethasone with pomalidomide and low-dose dexamethasone alone in patients with relapsed or refractory multiple myeloma (MM) who have received at least one prior treatment regimen with both lenalidomide and a proteasome inhibitor and have demonstrated disease progression. The study, which was conducted in collaboration with the European Myeloma Network, enrolled 304 participants.[10]

The primary endpoint is progression-free survival (PFS) between treatment arms. Secondary endpoints include rates of overall response rate (ORR), very good partial response (VGPR) or better, complete response (CR) or better and duration of response, among others.[10] The study reinforces findings from the Phase 1b EQUULEUS (MMY1001) trial, supported the U.S. Food and Drug Administration (FDA) approval of intravenous D-Pd in 2017 for the treatment of relapsed and refractory MM.[11] In November 2020, Janssen submitted regulatory applications to the U.S. FDA and European Medicines Agency (EMA) seeking approval of the combination of D-Pd for the treatment of patients with relapsed or refractory MM.

About daratumumab and daratumumab SC

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, it is estimated that nearly 190,000 patients have been treated with daratumumab worldwide.[12] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma (MM). Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[13]

CD38 is a surface protein that is highly expressed across MM cells, regardless of the stage of disease. Daratumumab SC binds to CD38 and induces myeloma 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.[14]

Data across nine Phase 3 clinical trials in the frontline and relapsed settings for MM and newly diagnosed light chain (AL) amyloidosis, have shown that daratumumab-based regimens resulted in significant improvement in progression free survival and/or overall survival.[15,16,17,18,19,20,21,22,23] Additional studies have been designed to assess the efficacy and safety of daratumumab SC in the treatment of other malignant and pre-malignant haematologic diseases in which CD38 is expressed.[24]

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

About AL Amyloidosis

Light chain (AL) amyloidosis is a rare and potentially fatal haematologic disorder that can affect the function of multiple organs.[1,2] The disease occurs when bone marrow produces abnormal antibodies called light chains, which clump together to form a substance called amyloid. These clumps of amyloid are deposited in tissues and vital organs and interfere with normal organ function, eventually causing organ deterioration.[1,2] AL amyloidosis is the most common type of systemic amyloidosis.[25] It frequently affects the heart, kidneys, digestive tract, liver and nervous system.[3] Diagnosis is often delayed and prognosis is poor due to advanced, multi-organ, particularly cardiac, involvement. Approximately 30,000 to 45,000 patients in the European Union and the United States have AL amyloidosis.[3]

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.[4] In Europe, more than 50,900 people were diagnosed with MM in 2020, and more than 32,500 patients died.[26] Around 50 percent of newly diagnosed patients do not reach five-year survival,[27] and almost 29 percent of patients with MM will die within one year of diagnosis.[28]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[6] Relapsed and refractory MM 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.[5]

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 Limited, Janssen Biologics B.V., and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

*Dr. Kastritis has served as a consultant to Janssen and 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 subcutaneous formulation for the treatment of patients with light chain amyloidosis. 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-Cilag Limited, Janssen Biologics B.V., 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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References

[1] Desport E, Bridoux F, Sirac C, Delbes S, Bender S, Fernandez B, Quellard N, Lacombe C, Goujon JM, Lavergne D, Abraham J. AL amyloidosis. Orphanet journal of rare diseases. 2012 Dec;7(1):54.
[2] Merlini G, Comenzo RL, Seldin DC, Wechalekar A, Gertz MA. Immunoglobulin light chain amyloidosis. Expert review of hematology. 2014 Feb 1;7(1):143-56.
[3] Lousada I, Comenzo RL, Landau H, et al. Light chain amyloidosis: patient experience survey from the Amyloidosis Research Consortium. Advances in Therapy. 2015;32(10):920-928.
[4] American Cancer Society. "What Is Multiple Myeloma?" Available at: http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma. Accessed June 2021.
[5] 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.
[6] 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.
[7] ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of Daratumumab in Combination With Cyclophosphamide, Bortezomib and Dexamethasone (CyBorD) Compared to CyBorD Alone in Newly Diagnosed Systemic Amyloid Light-chain (AL) Amyloidosis. NCT03201965. Available at: https://clinicaltrials.gov/ct2/show/NCT03201965. Last accessed: June 2021.
[8] Efstathios, K., & Merlini, G. (2021). Subcutaneous Daratumumab + Bortezomib, Cyclophosphamide, and Dexamethasone (VCd) in Patients With Newly Diagnosed Light Chain (AL) Amyloidosis: Updated Results From the Phase 3 ANDROMEDA Study. ASCO 2021.
[9] Dimopoulos, MA et al. APOLLO: Phase 3 Randomized Study of Subcutaneous Daratumumab Plus Pomalidomide and Dexamethasone (D-Pd) Versus Pomalidomide and Dexamethasone (Pd) Alone in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM).
[10] 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). Available at: https://clinicaltrials.gov/ct2/show/record/NCT03180736. Last accessed: June 2021.
[11] Chari A, Suvannasankha A, Fay JW, et al. Daratumumab plus pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma. *Blood*. 2017;130(8):974-981. doi:10.1182/blood-2017-05-785246.
[12] Janssen [data on file]. Number of patients treated with DARZALEX worldwide as of March 2021. RF-171498.

[13] Janssen EMEA. European Commission Grants Marketing Authorisation for DARZALEX®▼(Daratumumab) Subcutaneous Formulation for All Currently Approved Daratumumab Intravenous Formulation Indications. Available at: www.businesswire.com/news/home/20200604005487/en/European-Commission-Grants-Marketing-Authorisation-for-DARZALEX%C2%AE%E2%96%BC-daratumumab-Subcutaneous-Formulation-for-all-Currently-Approved-Daratumumab-Intravenous-Formulation-Indications. Last accessed: June 2021.
[14] European Medicines Agency. DARZALEX summary of product characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/darzalex-epar-product-information_en.pdf. Last accessed June 2020.
[15] Janssen Research & Development, LLC. A Study Comparing Daratumumab, Lenalidomide, and Dexamethasone With Lenalidomide and Dexamethasone in Relapsed or Refractory Multiple Myeloma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02076009?term=mmy3003&rank=1. Identifier: NCT02076009. Last accessed: June 2021.
[16] Janssen Research & Development, LLC. Addition of Daratumumab to Combination of Bortezomib and Dexamethasone in Participants With Relapsed or Refractory Multiple Myeloma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 [cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02136134?term=mmy3004&rank=1. Identifier: NCT02136134. Last accessed: June 2021.
[17] Janssen Research & Development, LLC. A Study to Evaluate Daratumumab in Transplant Eligible Participants With Previously Untreated Multiple Myeloma (Cassiopeia). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 [cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02541383?term=mmy3006. Identifier: NCT02541383. Last accessed: June 2021.
[18] Janssen Research & Development, LLC. 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 In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 [cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02195479?term=mmy3007&rank=1. Identifier: NCT02195479. Last accessed: June 2021.
[19] Janssen Research & Development, LLC. Study Comparing Daratumumab, Lenalidomide, and Dexamethasone With Lenalidomide and Dexamethasone in Participants With Previously Untreated Multiple Myeloma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 [cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT02252172?term=mmy3008&rank=1. Identifier: NCT02252172. Last accessed: June 2021.
[20] Janssen Research & Development, LLC. 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). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 [cited 2018 July 24]. Available at: https://clinicaltrials.gov/ct2/show/NCT03217812?term=MMY3011&rank=1. Identifier: NCT03217812. Last accessed: June 2021.
[21] European Myeloma Network. Compare Progression Free Survival Btw Daratumumab/Pomalidomide/Dexamethasone vs Pomalidomide/Dexamethasone (EMN14). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 [cited 2018 July 24] Available at: https://clinicaltrials.gov/ct2/show/NCT03180736?term=MMY3013&rank=2 Identifier: NCT03180736. Last accessed: June 2021.
[22] Amgen. Study of Carfilzomib, Daratumumab and Dexamethasone for Patients With Relapsed and/or Refractory Multiple Myeloma. (CANDOR). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 [cited 2018 July 24] Available at: https://clinicaltrials.gov/ct2/show/NCT03158688?term=NCT03158688&rank=1. Identifier: NCT03158688. Last accessed: June 2021.
[23] ClinicalTrials.Gov. A Study to Evaluate the Efficacy and Safety of Daratumumab in Combination With Cyclophosphamide, Bortezomib and Dexamethasone (CyBorD) Compared to CyBorD Alone in Newly Diagnosed Systemic Amyloid Light-chain (AL) Amyloidosis. Available at: https://clinicaltrials.gov/ct2/show/NCT03201965. Last accessed: June 2021.

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[24] ClinicalTrials.Gov. A Study of Subcutaneous Daratumumab Versus Active Monitoring in Participants With High-Risk Smoldering Multiple Myeloma. Available at: https://clinicaltrials.gov/ct2/show/NCT03301220. Last accessed: June 2021.
[25] National Organization for Rare Disorders. Amyloidosis. Available at: https://rarediseases.org/rare-diseases/amyloidosis/. Last accessed June 2021.
[26] GLOBOCAN 2020. Cancer Today Population Factsheets: Europe Region. Available at: https://gco.iarc.fr/today/data/factsheets/populations/908-europe-fact-sheets.pdf. Last accessed: June 2021.
[27] Cancer.Net. Multiple Myeloma: Statistics. Available at: https://www.cancer.net/cancer-types/multiple-myeloma/statistics. Last accessed: June 2021.
[28] Jung SH et al., Risk factors associated with early mortality in patients with multiple myeloma who were treated upfront with a novel agents containing regimen. BMC Cancer. 2016;16:613.
[29] 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.
[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: June 2021.