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News Release

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Janssen Receives Two Positive CHMP Opinions Recommending Expanded Use of DARZALEX®▼ (daratumumab) Subcutaneous (SC) Formulation for New Indications in Europe

Daratumumab SC in combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd) demonstrated significantly higher complete response rate in newly diagnosed patients with light chain (AL) amyloidosis compared to VCd alone

The addition of daratumumab SC to pomalidomide and dexamethasone (D-Pd) resulted in significantly higher progression-free survival (PFS) in patients with pre-treated multiple myeloma (MM) compared to Pd alone

BEERSE, BELGIUM, 21 May, 2021 - The Janssen Pharmaceutical Companies of Johnson & Johnson today announced 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) subcutaneous (SC) formulation in two new indications. One recommendation is for the use of daratumumab SC in combination with cyclophosphamide, bortezomib and dexamethasone (D-VCd), for the treatment of adult patients with newly diagnosed systemic light chain (AL) amyloidosis. The second is for the use of daratumumab SC in combination with pomalidomide and dexamethasone (D-Pd) for the treatment of adult patients 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 diseases progression on or after the last therapy.

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Both AL amyloidosis and relapsed MM are blood disorders for which unmet treatment needs remain.[1,2] AL amyloidosis is a rare and potentially life-threatening disorder that occurs when an insoluble protein called amyloid builds up in tissues and organs, and eventually causes organ deterioration.[1,3] The broad and often nonspecific nature of symptoms associated with AL amyloidosis can lead to delays in diagnosis, resulting in organ function deterioration having advanced by the time treatment is initiated for a proportion of patients.[4,5] In Europe, there are currently no approved treatments for AL amyloidosis. Without treatment, the average survival rate is 12–18 months, and only around six months for those with severely impaired heart function.[6]

Multiple myeloma, despite significant treatment advances over the last decade, remains a complex blood cancer to treat, with a particularly challenging area being the management of relapsed or refractory disease. Patient outcomes worsen with each relapse, and the need for effective treatment options becomes crucial.[2,7]

"Today's news is an important step forward in enabling us to meet the treatment needs of more patients with these complex blood disorders. Daratumumab has played a significant role in transforming the treatment landscape for multiple myeloma and has now been used to treat nearly 190,000 patients since its first approval in 2016," said Saskia De Haes, Vice President, EMEA Regulatory Affairs, Janssen Pharmaceutica NV. "We look forward to harnessing our expertise to deepen our impact in multiple myeloma and bring transformation to patients with AL amyloidosis, a disease area where the need for innovation is imperative."

The Positive CHMP Opinion for the AL amyloidosis indication is supported by data from the Phase 3 ANDROMEDA study.[8] The study evaluated daratumumab SC in combination with 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 compared to patients treated with VCd alone (53.3 percent for D-VCd and 18.1 percent for VCd; $P<0.0001$). Overall, D-VCd had a safety profile consistent with that previously observed for each of the agents alone.[8]

The Positive CHMP Opinion for daratumumab SC in combination with Pd in the treatment of MM is supported by data from the Phase 3 APOLLO study conducted in collaboration with the European Myeloma Network.[9] The study compared D-Pd with Pd alone in 304 patients with relapsed or refractory MM who have received at least one prior treatment regimen with both

lenalidomide and a proteasome inhibitor.[9] Results show that the addition of daratumumab significantly reduced the risk of progression or death by 37 percent, compared to Pd alone (hazard ratio, 0.63; 95 percent confidence interval, 0.47-0.85; *P*=0.0018).[9] The median progression-free survival (PFS) for the D-Pd vs. Pd arms was 12.4 vs. 6.9 months, respectively.[9] Response rates were significantly higher with D-Pd compared to Pd alone, including rates of overall response (69 percent vs. 46 percent), rates of very good partial response (VGPR) or better (51 percent vs. 20 percent), the rate of complete response (CR) (25 percent vs. 4 percent) and the rate of minimal residual disease-negativity (9 percent vs. 2 percent). The safety profile of D-Pd has been shown to be consistent with known profiles of daratumumab SC and Pd.[9]

Data from the ANDROMEDA and APOLLO studies were presented most recently during the American Society of Hematology (ASH) 2020 Annual Meeting.[8,9]

"At Janssen, our goal is to improve and prolong patients' lives as we continue our work to advance oncology science and ultimately deliver cures," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "We continually investigate new uses of daratumumab to expand on the ways in which it can deliver benefit to various patient populations."

Both Positive Opinions will now be reviewed by the European Commission (EC), which has the authority to grant final approval of the indications.

#ENDS#

About the ANDROMEDA Study[10]

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.[10]

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About the APOLLO Study[11]

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.[11]

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. 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.[12] 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.[11]

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.[13] 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.[14]

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.[15]

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.[16,17,18,19,20,21,22,23,24] 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.[25]

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.[1,3] 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.[1,3] AL amyloidosis is the most common type of systemic amyloidosis.[26] It frequently affects the heart, kidneys, digestive tract, liver and nervous system.[1,3] 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.[27]

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.[28] In Europe, more than 50,900 people were diagnosed with MM in 2020, and more than 32,500 patients died.[29] Around 50 percent of newly diagnosed patients do not reach five-year survival,[30,31] and almost 29 percent of patients with MM will die within one year of diagnosis.[32]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[2] 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.[33] 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.[34] 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.[7]

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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 Research & Development, LLC, Janssen Pharmaceutica NV and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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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 Research & Development, LLC, Janssen Pharmaceutica NV, 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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