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European Commission Approves Darzalex®▼ (daratumumab) in Combination with Bortezomib, Thalidomide and Dexamethasone (VTd) for Patients with Newly Diagnosed Multiple Myeloma Who Are Transplant Eligible

- *Daratumumab-VTd is the first regimen approved in over six years for newly diagnosed patients who are eligible for a stem cell transplant*[1]
- *Approval is based on data from the Phase 3 CASSIOPEIA trial, which demonstrated that the addition of daratumumab resulted in deeper response rates and improved progression-free survival (PFS) compared to VTd alone*[2]
- *Daratumumab has been used to treat more than 100,000 patients worldwide*[3]
- *This is the sixth approval for daratumumab and the third in the frontline setting*[4]

BEERSE, BELGIUM, 20 January 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the European Commission (EC) has granted marketing authorisation for Darzalex® (daratumumab) in combination with bortezomib, thalidomide and dexamethasone (VTd) for the treatment of patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (ASCT). This approval is based on results from Part one of the Phase 3 CASSIOPEIA (MMY3006) study, published in *The Lancet*[5] in June 2019 and presented at the 2019 American Society of Clinical Oncology (ASCO) Meeting.

"The effectiveness of first-line treatment is critical to maximise time until relapse. So, we asked ourselves, can we improve the standard of care that is bortezomib, thalidomide and dexamethasone (VTd) to provide patients with valuable extra time?" said Philippe Moreau, M.D., principal investigator and Head of the Haematology Department at the University Hospital of Nantes, France. "The CASSIOPEIA study answered that question definitively, demonstrating that the addition of daratumumab in combination with VTd can lead to very

deep remissions and also prolong PFS. I'm pleased to see the European Commission have recognised this as well."

"Today's approval marks the first opportunity for newly diagnosed, transplant eligible patients to be treated with a monoclonal antibody, and the first new treatment for this patient population in over six years," said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag. "We are thrilled that newly diagnosed patients with multiple myeloma and their doctors will have a long-awaited additional frontline therapy."

The Phase 3 CASSIOPEIA trial is a two-part study. Results from this first part of the trial showed that after consolidation, the stringent complete response (sCR) rate was significantly higher in the daratumumab-VTd arm (29 percent) compared to VTd alone (20 percent) (Odds Ratio [OR] = 1.60; 95 percent confidence interval [CI], 1.21-2.12; P<0.0010).[2] At a median follow-up of 18.8 months, PFS was significantly improved in the daratumumab-VTd group compared to VTd alone (Hazard Ratio [HR] = 0.47; 95 percent CI, 0.33-0.67; P<0.0001), and the median PFS was not reached in either arm.[2] The addition of daratumumab to VTd resulted in an 18-month PFS rate of 93 percent compared to 85 percent for VTd alone.[2]

The most common (≥10%) Grade 3/4 treatment-emergent adverse events (TEAEs) for daratumumab-VTd and VTd, respectively, were neutropenia (28 percent vs. 15 percent), lymphopenia (17 percent vs. 10 percent), stomatitis (13 percent vs. 16 percent) and thrombocytopenia (11 percent vs. 7 percent).[2] In the daratumumab-VTd combination arm, infusion-related reactions occurred in 35 percent of patients.[2]

"This approval represents our commitment to investigate daratumumab in earlier disease stages of multiple myeloma and to develop more effective frontline treatment options for newly diagnosed patients who are eligible for transplantation," adds Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC.

#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 Trial[6]

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-class[7] biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[8] 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.[3] 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.[6,9,10,11,12,13,14,15] 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.[16,17] 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.[18]

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.[19] In Europe, more than 48,200 people were diagnosed with MM in 2018, and more than 30,800 patients died.[20] Almost 60 percent of patients with MM do not survive more than five years after diagnosis.[21]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[22] Refractory MM is when a patient's disease progresses within 60 days of their last therapy.[23,24] Relapsed cancer is when the disease has returned after a period of initial, partial or complete remission.[25] 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.[26] Patients who relapse after treatment with standard therapies, including proteasome inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[27]

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.

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