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Janssen Seeks EMA Approval for Novel Subcutaneous Formulation of DARZALEX®▼ (daratumumab)

Data supporting the application demonstrated that the investigational subcutaneous formulation improved quality of life, reduced administration time, lowered rates of infusion-related reactions, and was non-inferior compared to intravenous administration[1]

BEERSE, BELGIUM, 19 July 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of an extension application to the European Medicines Agency (EMA) for subcutaneous (under the skin) use of DARZALEX® (daratumumab) for the treatment of patients with multiple myeloma. This subcutaneous formulation of daratumumab is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20) [Halozyme's ENHANZE® drug delivery technology]. Daratumumab is currently only approved for intravenous (IV) use.

"This new formulation is an example of our unwavering commitment to pursue innovative treatment options to support people living with multiple myeloma," said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag. "Importantly, subcutaneous daratumumab demonstrated comparable efficacy with the existing IV formulation, reduced the rate of infusion-related reactions and significantly shortened the time it takes for patients to receive treatment, from several hours to approximately five minutes."

The submission is supported by two studies, the Phase 2 PLEIADES (MMY2040) study and the Phase 3 COLUMBA (MMY3012) study recently presented at the 24th European Hematology Association (EHA) Congress, and at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting where the data were selected for the Best of ASCO 2019 Meetings, which highlight practice-changing science and leading research in oncology.[1,2]

"Janssen has an extensive heritage in multiple myeloma and we are committed to developing innovative approaches to minimise the treatment burden for patients with multiple myeloma," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "We look forward to working with the EMA in its review of the data supporting this application."

Janssen has also submitted a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) seeking approval of the new daratumumab subcutaneous formulation.

In Europe, daratumumab is indicated:[3]

- in combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant
- 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
- 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.

#ENDS#

About the COLUMBA Trial (NCT03277105)[4]

The randomised, open-label, multicentre Phase 3 study included 522 patients with multiple myeloma 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 (median age of 67). In the arm that received the subcutaneously (SC) administered formulation of daratumumab (n=263), patients 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 daratumumab IV arm (n=259), patients received daratumumab for intravenous infusion 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 objective response rate (ORR) (analysed by Farrington-Manning test, with non-inferiority = 60 percent retention of ORR) and pre-dose C3D1 daratumumab C_{trough} (non-inferiority = lower bound of 90 percent confidence interval (CI) for the ratio of the geometric means [GM] ≥80%).

About the PLEIADES Trial (MMY2040)[2]

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

About daratumumab

Daratumumab is a first-in-class[5] biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[6] 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.[3] A subset of myeloid derived suppressor cells (CD38+ MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by daratumumab.[3] Since launch, it is estimated that daratumumab has treated 90,000 patients worldwide.[7] 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.[8,9,10,11,12,13,14,15] 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 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 Biotech, Inc. and Janssen Research & Development, LLC 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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