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Janssen Submits Application to the European Medicines Agency (EMA) to Expand Use of DARZALEX®▼(daratumumab) to Include Combination with Standard of Care Regimens

Phase 3 data supporting submission suggests potential clinical benefit of daratumumab as a backbone therapy in combination with either a proteasome inhibitor (PI) or an immunomodulatory agent for relapsed multiple myeloma patients

BEERSE, BELGIUM, 23 August, 2016 – Janssen-Cilag International NV today announced the submission of a Type II variation application to the European Medicines Agency (EMA), seeking to broaden the existing marketing authorisation for the immunotherapy DARZALEX®▼(daratumumab) to include treatment of adult patients with relapsed multiple myeloma who have received at least one prior therapy. The expanded indication is based on daratumumab in combination with lenalidomide (an immmunomodulatory agent) and dexamethasone, or bortezomib (a PI) and dexamethasone.

Daratumumab is currently approved by the European Commission (EC) for monotherapy of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a PI and an immunomodulatory agent, and who have demonstrated disease progression on the last therapy.[1]

"Despite remarkable advances over recent years, multiple myeloma remains an incurable illness. We are therefore excited to take an important step forward in further realising the potential of daratumumab, and its possible benefit as a backbone therapy in multiple myeloma treatment," said Jane Griffiths, Company Group Chairman, Janssen Europe,

Middle East and Africa. "We look forward to working closely with the EMA throughout the review process and remain committed to exploring the full clinical benefit of this compound for patients who are awaiting new options."

The regulatory submission is now pending validation by the EMA and is primarily supported by data from two Phase 3 studies, in patients with multiple myeloma who have received one or more prior lines of therapy, showing combination of daratumumab with a PI or immunomodulatory agent resulted in a >60% reduction in the risk of disease progression or death.[2,3]

- The MMY3004 (CASTOR) clinical trial evaluated daratumumab in combination with bortezomib and dexamethasone, compared to bortezomib and dexamethasone alone. Study results were previously presented at the 52nd Annual Meeting of the American Society of Clinical Oncology (ASCO) and at the 21st Annual Congress of the European Hematology Association (EHA) in June 2016.[2]
- The MMY3003 (POLLUX) clinical trial evaluated daratumumab in combination with lenalidomide and dexamethasone, compared to lenalidomide and dexamethasone alone. Findings were presented at EHA in June 2016.[3]

The submission also included data from the Phase 1 study of daratumumab in combination with pomalidomide and dexamethasone in patients who received at least two prior lines of therapy. More information on these trials can be found at www.clinicaltrials.gov (NCT02076009, NCT02136134 and NCT01998971).

The Type II variation application follows the recent submission to the U.S. Food and Drug Administration (FDA) of a supplemental Biologics License Application for daratumumab in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone for treatment of patients with multiple myeloma who have received at least one prior therapy. In addition, on 25 July, 2016 Janssen announced that the FDA granted a Breakthrough Therapy Designation for daratumumab in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy. This marks the second Breakthrough Therapy Designation for daratumumab in the U.S., which is intended to expedite the development and review timelines of potential new medicines to treat serious or life-threatening diseases, where preliminary clinical evidence shows that the medicine may provide substantial improvement over existing therapies.[4]

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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.[5] MM is the second most common form of blood cancer, with around 39,000 new cases worldwide in 2012.[6] MM most commonly affects people over the age of 65 and is more common in men than in women.[7] The most recent five-year survival data for 2000-2007 show that across Europe, up to half of newly diagnosed patients do not reach five-year survival.[8] Almost 29% of patients with MM will die within one year of diagnosis.[9] Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure. 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.[7] Patients who relapse after treatment with standard therapies, including PIs and immunomodulatory agents, have poor prognoses and few treatment options available.[10]

About Daratumumab

Daratumumab is a first-in-class biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[11-13] Daratumumab induces rapid tumour cell death through apoptosis (programmed cell death)[1,14] and multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).[1,15,16] Daratumumab has also demonstrated immunomodulatory effects that contribute to tumour cell death via a decrease in immune suppressive cells including T-regs, B-regs and myeloid-derived suppressor cells.[1,17] Daratumumab is being evaluated in a comprehensive clinical development programme that includes five Phase 3 studies across a range of treatment settings in multiple myeloma. Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant diseases in which CD38 is expressed. For more information, please see www.clinicaltrials.gov.

The most frequently reported adverse reactions are infusion-related reactions (IRRs) (48%). Other frequently reported adverse reactions (≥ 20%) were fatigue (39%), pyrexia (21%), cough (21%), nausea (27%), back pain (23%), upper respiratory tract infection (20%), anaemia (27%), neutropenia (22%) and thrombocytopenia (20%).[1] For further

information, please see www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/004077/WC500207296.pdf.

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.

About the Janssen Pharmaceutical Companies

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA.

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 potential benefits of, and expanded indication for, DARZALEX® (daratumumab). 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-Cilag International NV, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: the uncertainties inherent in product 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 or financial distress 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 description 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, 2016, including in Exhibit 99 thereto, 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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