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CHMP Issues a Positive Opinion on Janssen's Single-Agent DARZALEX® (daratumumab)

First-in-class monoclonal antibody targeting CD38 for the treatment of multiple myeloma

BEERSE, BELGIUM, 01 April, 2016 – Janssen-Cilag International NV ("Janssen") announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a Positive Opinion recommending a conditional marketing authorisation for first-in-class CD38 immunotherapy DARZALEX® (daratumumab) in the European Union. The recommended indication is for monotherapy of adult patients with relapsed and refractory multiple myeloma (MM), whose prior therapy included a proteasome inhibitor (PI) and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.[1] This application was reviewed under an accelerated assessment by the CHMP, a process reserved for medicinal products expected to be of major public health interest, particularly from the point of view of therapeutic innovation.

MM is a blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow.[2] In cases of refractory MM, the disease has progressed on or within 60 days of the last therapy.[3] The prognosis for patients with relapsed and refractory MM remains poor. For patients with refractory MM, the median overall survival (OS) ranges from nine months to only five months.[4]

The Opinion of the CHMP was based on a review of data from the Phase 2 MMY2002 (SIRIUS) study, published in *The Lancet*,[5] the Phase 1/2 GEN501 study, published in *The*

New England Journal of Medicine,[6] and data from three additional supportive studies. These studies included heavily pre-treated patients with relapsed and refractory multiple myeloma who had exhausted other approved treatment options and whose disease was progressive at enrolment. Findings from a combined efficacy analysis of the GEN501 and MMY2002 (SIRIUS) trials demonstrated that after a mean follow-up of 14.8 months, the estimated median OS for single-agent daratumumab (16 mg/kg) in these heavily pre-treated patients was 20 months (95 percent CI, 15-not estimable). The overall response rate (ORR) for the combined analysis was 31 percent, and 83 percent of patients achieved stable disease or better.[7]

Daratumumab is the first CD38-directed monoclonal antibody (mAb) recommended for approval in Europe. It works by binding to CD38, a signalling molecule highly expressed on the surface of multiple myeloma cells regardless of stage of disease. In doing so, daratumumab triggers the patient's own immune system to attack the cancer cells, resulting in rapid tumour cell death through multiple, immune-mediated mechanisms of action and through immunomodulatory effects, in addition to direct tumour cell death via apoptosis (programmed cell death).[8-11]

"We are committed to delivering innovative new therapies to patients living with complex blood cancers, and have been working closely with the CHMP on the submission of daratumumab to ensure the assessment could be completed under the accelerated timeline," said Jane Griffiths, Company Group Chairman, Janssen Europe, Middle East and Africa. "We are delighted to receive this Positive Opinion, which brings us one step closer to making daratumumab available to multiple myeloma patients in Europe."

The CHMP's Positive Opinion will now be reviewed by the European Commission, which has the authority to grant marketing authorisation for medicines in the European Economic Area. The European Commission's final decision on daratumumab is anticipated in the coming months.

This announcement follows daratumumab being granted its first regulatory approval by the U.S. Food and Drug Administration (FDA) for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy, including a PI and an immunomodulatory agent, or who are double-refractory to a PI and an immunomodulatory agent, in November 2015 after a four month Priority Review by the FDA.[9]

Janssen has exclusive worldwide rights to the development, manufacturing and commercialisation of daratumumab for all potential indications. Janssen licensed daratumumab from Genmab A/S in August 2012.

#ENDS#

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.[2] MM is the second most common form of blood cancer, with around 39,000 new cases worldwide in 2012.[12] MM most commonly affects people over the age of 65 and is more common in men than in women.[13] Across Europe, five-year survival rates are 23 percent to 47 percent of people diagnosed.[14] Almost 29 percent of patients with MM will die within one year of diagnosis.[15] 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 which can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[13] Patients who relapse after treatment with standard therapies, including PIs and immunomodulatory agents, have poor prognoses and few treatment options available.[16]

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.[17] Daratumumab induces rapid tumour cell death through apoptosis (programmed cell death)[9,10] and multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).[8,9,11] Daratumumab has also demonstrated immunomodulatory effects that contributes to tumour cell death via a decrease in immune suppressive cells including T-regs, B-regs and myeloid-derived suppressor cells.[18] Five Phase 3 clinical studies with daratumumab in relapsed and frontline settings are currently ongoing. Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant diseases on which CD38 is expressed. For more information, please see www.clinicaltrials.gov.

About MMY2002 (SIRIUS) and GEN501

These studies included heavily pre-treated patients with relapsed and refractory multiple myeloma who had exhausted other approved treatment options and whose disease was progressive at enrolment. Safety data from the MMY2002 (SIRIUS) and GEN501 trials suggested that daratumumab (16 mg/kg) has a favourable and clinically manageable safety profile as a monotherapy.[5,6]

In the MMY2002 (SIRIUS) trial, no patients discontinued treatment due to infusion-related reactions (IRRs) and only five patients (5 percent) discontinued treatment due to adverse events (AEs) (all grade), none of which were considered drug-related.[5] AEs, which occurred in less than 20 percent of patients, were fatigue (40 percent), anaemia (33 percent), nausea (29 percent), thrombocytopenia (25 percent), back pain (22 percent), neutropenia (23 percent) and cough (21 percent).[5] Infusion-related reactions (IRR) were reported in 42 percent of patients and were predominantly grade 1 or 2 (5 percent grade 3; no grade 4 reported).[5] These occurred mainly during the first infusion. The most common IRRs included nasal congestion (12 percent), throat irritation (7 percent), cough, dyspnoea, chills, and vomiting (6 percent each)[5] – all of which were treated with standard of care and slower infusion rates.[19]

In the GEN501 trial, serious AEs occurred in 33 percent of patients in the cohort that received 16 mg/kg in part 2 of the study.[6] Infusion-related reactions (IRRs) occurred in 71 percent of patients in the 8 mg/kg and 16 mg/kg cohorts, and all were grades 1 and 2, with the occurrence of one patient with grade 3 reactions.[6] The majority of IRRs occurred during the first infusion, with notably fewer during subsequent infusions.[6] No patient discontinued treatment due to an IRR. The most common AEs in either treatment group were fatigue, allergic rhinitis, and pyrexia (fever).[6] The most frequent haematologic AE was neutropenia (abnormally low levels of neutrophils, a type of white blood cell), which occurred in 12 percent of patients (n=5) in the 16 mg/kg cohort.[6] Grade 3 or 4 AEs were reported in 26 percent of patients in the 16 mg/kg cohort, with pneumonia (n=5) and thrombocytopenia (abnormally low levels of platelets in the blood; n=4) as the most common in both the 8 mg/kg and 16 mg/kg cohorts.[6]

About Janssen

The Janssen Pharmaceutical Companies of Johnson & Johnson are dedicated to addressing and solving the most important unmet medical needs of our time, including oncology (e.g., multiple myeloma and prostate cancer), immunology (e.g., psoriasis),

neuroscience (e.g., schizophrenia, dementia and pain), infectious disease (e.g., HIV/AIDS, hepatitis C and tuberculosis), and cardiovascular and metabolic diseases (e.g., diabetes). Driven by our commitment to patients, we develop sustainable, integrated healthcare solutions by working side-by-side with healthcare stakeholders, based on partnerships of trust and transparency. More information can be found on www.janssen.com/EMEA. Follow us on www.twitter.com/janssenEMEA for our latest news.

Cilag GmbH International; Janssen Biotech, Inc.; and Janssen-Cilag International NV are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Janssen in Oncology

Our goal is to fundamentally alter the way cancer is understood, diagnosed and managed, reinforcing our commitment to the patients who inspire us. In looking to find innovative ways to address the cancer challenge, our primary efforts focus on several treatment and prevention solutions. These include a focus on haematologic malignancies, prostate cancer and lung cancer; cancer interception with the goal of developing products that interrupt the carcinogenic process; biomarkers that may help guide targeted, individualised use of our therapies; as well as safe and effective identification and treatment of early changes in the tumour microenvironment.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development, including potential regulatory approval of a new product. 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 International NV, 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 development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; competition, including technological advances, new products and patents attained by competitors; challenges to patents; manufacturing difficulties or delays; product efficacy or safety concerns resulting in product recalls or regulatory action; 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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