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New Data for Darzalex®▼(daratumumab) Presented at ASH 2017 Show Feasibility of Subcutaneous Use and Potential of Darzalex as a Treatment for Smouldering Multiple Myeloma

Early data evaluated subcutaneous delivery of daratumumab in relapsed or refractory multiple myeloma patients (Abstract #838)

New Phase 2 data investigated single-agent daratumumab for intermediate or high-risk smouldering multiple myeloma (Abstract #510)

BEERSE, BELGIUM, December 12, 2017 – Janssen-Cilag International NV ("Janssen") today announced new data from the Phase 1b PAVO clinical study, which demonstrated that the subcutaneous delivery of Darzalex® (daratumumab) co-formulated with recombinant human hyaluronidase enzyme (daratumumab-SC), was generally well-tolerated, with a 12 percent rate of infusion-related reactions (IRRs), in patients with relapsed or refractory multiple myeloma.[1] These data were featured as an oral presentation at the 59th American Society of Hematology (ASH) Annual Meeting in Atlanta. Daratumumab is currently approved for intravenous (IV) administration, and results from the PAVO trial serve as the basis for an actively enrolling Phase 3 study comparing subcutaneous administration of daratumumab over 3-5 minutes with the approved IV administration in relapsed and refractory multiple myeloma patients.[2]

Daratumumab is currently indicated for use 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;[3] and as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor

(PI) and an immunomodulatory agent, and who have demonstrated disease progression on the last therapy.[3]

Additionally, results from the Phase 2 CENTAURUS clinical study showed daratumumab monotherapy had a generally well-tolerated safety profile in patients with intermediate or high-risk smouldering multiple myeloma, with the most common treatment-emergent adverse events (TEAEs) being fatigue, cough, upper respiratory tract infection, headache and insomnia.[4] These data were featured as an oral presentation on December 10 (Abstract #510).[5] Smouldering multiple myeloma is an asymptomatic precursor stage to multiple myeloma where early intervention to delay the progression to active disease may potentially benefit patients.[4,5] These results serve as the basis for an actively enrolling Phase 3 study for daratumumab vs. observation in smouldering multiple myeloma.[6]

Key Safety Findings from PAVO Study

Updated data from Part 2 of the open-label, multicentre, dose-finding Phase 1b PAVO (MMY1004) study showed the initial safety and efficacy of daratumumab co-formulated with recombinant human hyaluronidase enzyme (rHuPH20) delivered by manual subcutaneous injection (daratumumab-SC).[7] IRRs were reported in 12 percent of patients receiving daratumumab-SC 1800 mg,[1] with no Grade 4 IRRs reported.[1] Subcutaneous administration was generally well-tolerated in the daratumumab-SC 1800 mg cohort, with 20 percent of patients experiencing reversible and short-lasting erythema (measurable erythema or induration are all reversible within 1 to 2 hours) at the injection site.[1]

In the daratumumab-SC 1800 mg cohort, drug-related TEAEs occurred in 48 percent of patients; the most common TEAEs included lymphopenia, thrombocytopenia, insomnia and pyrexia.[1] Data for this new investigational delivery method demonstrated the subcutaneous administration of daratumumab and rHuPH20 was generally well-tolerated, with rates of IRRs lower than those observed with IV administration of daratumumab.[7] Additionally, an overall response rate (ORR) of 44 percent was observed in the daratumumab-SC 1800 mg cohort, with a median follow up of 4.6 months.[1]

“The PAVO study demonstrated daratumumab-SC, is also generally well-tolerated in patients, with the added advantage of shorter infusion times and lower risk of infusion-related reactions,” said Dr Catherine Taylor, Haematology Therapeutic Area Lead, Janssen Europe, Middle East and Africa (EMEA). “The results support the continued study of daratumumab delivered subcutaneously, with a

Phase 3 study already underway to fully understand the benefits to patients and the healthcare community."

Key Findings from CENTAURUS Study

Preliminary data presented from the randomised, open-label, Phase 2 CENTAURUS (SMM2001) study evaluated three dosing schedules for daratumumab monotherapy in patients with intermediate or high-risk smouldering multiple myeloma.[5] A total of 123 patients were randomised to one of three treatment arms receiving daratumumab 16 mg/kg intravenously in eight-week cycles: 1.) a long-intense dosing schedule (LONG) where daratumumab was administered weekly in Cycle 1, every other week in Cycle 2-3, every four weeks in Cycle 4-7, and every eight weeks up to Cycle 20; 2.) an intermediate dosing schedule (INT), where daratumumab was given weekly in Cycle 1, and every eight weeks up to Cycle 20 and; 3.) a short intense dosing schedule (SHORT), where daratumumab was given weekly for one cycle.[5]

Study findings indicated that daratumumab was generally well-tolerated, with a safety profile comparable to daratumumab in the relapsed or refractory multiple myeloma setting. Haematologic TEAEs occurred in less than 10 percent of patients across all arms. Rates of Grade 3/4 infection were less than or equal to five percent in all arms.[5] Any-grade IRRs occurred in 56 percent, 42 percent and 55 percent of patients in the LONG, INT and SHORT dosing cohorts, respectively.[4,5] At the time of clinical cut-off, one death due to disease progression in the short dosing cohort was confirmed.[4,5] With a median follow-up of 15.8 months (range, 0.0-23.9), the ORR was numerically higher in the LONG arm than in INT or SHORT arms (56 percent, 54 percent and 38 percent, respectively).[4] The estimated 12-month PFS rates were 95 percent, 88 percent and 81 percent in the LONG, INT and SHORT arms, respectively.[4]

"These early results are encouraging, demonstrating the potential of daratumumab in tackling multiple myeloma, by treating smouldering multiple myeloma, a precancerous form of the disease," Niels van de Donk, MD, PhD, with the Department of Hematology, VU University Medical Centre. "Our aim is to delay or even prevent the evolution of this premalignant condition into active disease."

#ENDS#

About Daratumumab for Intravenous Infusion

Daratumumab for intravenous use is a first-in-class biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[8,9,10] 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 (MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by daratumumab.[3] Daratumumab is being evaluated in a comprehensive clinical development program across a range of treatment settings in multiple myeloma, such as in frontline and relapsed settings.[2,11-18] Additional studies are ongoing or planned to assess its potential for a solid tumour indication and in other malignant and pre-malignant diseases in which CD38 is expressed, such as smouldering myeloma.[19-22] For more information, please see www.clinicaltrials.gov.

For further information on daratumumab, please see the Summary of Product Characteristics at http://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.[23]

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.[24] MM is the second most common form of blood cancer, with around 39,000 new cases worldwide in 2012.[25] MM most commonly affects people over the age of 65 and is more common in men than in women.[26] 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.[27] Almost 29% of patients with MM will die within one year of diagnosis.[28]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[29] 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.[30] Patients who relapse after treatment with standard therapies, including PIs and immunomodulatory agents, have poor prognoses and few treatment options available.[31]

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 for our latest news.

Cilag GmbH International; Janssen Biotech, Inc.; Janssen Oncology, Inc. and Janssen-Cilag International NV 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 implications of data from two clinical studies evaluating DARZALEX® (daratumumab), including feasibility of alternative dosing approaches and the potential of DARZALEX as a treatment for smoldering 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 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 research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success for new products and indications; 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 behavior 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 1, 2017, including under "Item 1A. Risk Factors," its most recently filed Quarterly Report on Form 10-Q, including under the caption "Cautionary Note Regarding Forward-Looking Statements," 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 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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