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Daratumumab Combined with Standard Treatment for Multiple Myeloma Produced Deep and Durable Responses in Relapsed or Refractory Patients

Results featured at the 57th Annual American Society of Hematology Meeting and Exposition:

- *72 percent of relapsed or refractory multiple myeloma patients treated with daratumumab combination therapy did not progress or relapse after 18 months of treatment (GEN 503)*
- *Daratumumab in combination with pomalidomide and dexamethasone produced rapid, deep and durable responses in relapsed and refractory multiple myeloma patients who had received at least two (median of 3.5) prior lines of therapy, including two or more consecutive cycles of lenalidomide and bortezomib, and were refractory to their last line of treatment (MMY1001 Phase1b)*
- *Single-agent daratumumab demonstrated a median overall survival of 20 months in heavily pre-treated relapsed and refractory multiple myeloma patients who have exhausted other approved treatment options. A partial response or better was achieved by 31 percent of patients, and 83 percent achieved stable disease or better (GEN 501 & MMY2002)*

BEERSE, BELGIUM, December 6, 2015 – Janssen-Cilag International NV announced new data from the ongoing Phase 1/2 GEN503 investigational study showing the human CD38-directed monoclonal antibody daratumumab, in combination with lenalidomide and dexamethasone, yielded an overall response rate (ORR) of 81 percent in relapsed or refractory multiple myeloma patients who had received a median of two prior therapies. After 18 months of treatment, investigators observed an overall survival (OS) rate of 90 percent, with 72 percent of patients experiencing progression-free survival (PFS).[1]

The data, from the cohort expansion phase of GEN503, were presented today during the official press programme at the 57th Annual American Society of Hematology (ASH) Meeting and Exposition in Orlando, FL, U.S. and will be presented in full during an oral abstract session on Monday, December 7 at 7:30 a.m. Eastern Time (ET) / 1:30 p.m. Central European Time (CET).

“Daratumumab has already shown pronounced activity as a single-agent immunotherapy in a heavily pre-treated patient population with relapsed and refractory multiple myeloma. These findings suggest that it has the potential to induce rapid, deep, and durable responses in combination with standard treatment in earlier lines of therapy,” said lead study author, Professor Torben Plesner, Department of Hematology, Vejle Hospital, Vejle, Denmark. “These data are particularly exciting, as 72 percent of patients treated with daratumumab combination therapy did not progress or relapse after 18 months of treatment.”

The cohort expansion phase of the open label, international, multicentre, dose escalating Phase 1/2 GEN503 study enrolled 32 patients who had received a median of two prior lines of therapy. Stringent complete response (sCR) was reported in 25 percent of patients (n=8), complete response (CR) was reported in 9 percent (n=3), very good partial response (VGPR) was reported in 28 percent (n=9), and partial response (PR) was reported in 19 percent (n=6). Among all patients, the median times to first and best response were one month (95 percent confidence interval [CI], 0.5-5.6) and 5.1 months (95 percent CI, 0.5-14.4), respectively. The median duration of response was not reached.[1]

“Daratumumab is currently undergoing regulatory review by the European Medicines Agency (EMA) as monotherapy for relapsed and refractory multiple myeloma in heavily pre-treated patients. These new data indicate its potential as a treatment option for relapsed or refractory multiple myeloma in combination with standard treatments. Janssen strongly believes our robust clinical trial programme will allow us to unlock the full potential of this first human CD38-directed monoclonal antibody, both as a single agent and in combination with standard treatment,” said Jane Griffiths, Company Group Chairman, Janssen Europe, Middle East and Africa. “It’s very exciting to see such compelling data as part of more than 40 company-sponsored abstracts being presented at ASH this year.”

The two-part GEN503 study is comprised of a dose escalation study (part 1) and a cohort expansion study (part 2). In part 1, patients received daratumumab in combination with lenalidomide (25 mg orally on days 1 through 21 of every 28-day cycle) and dexamethasone (40 mg intravenously and orally once weekly). Daratumumab 2-16 mg/kg body weight was administered as an intravenous infusion given weekly for the first eight weeks, then bi-weekly (every two weeks) for the next 16 weeks, and then monthly until disease progression or unmanageable toxicity for 24 months in total. In

part 2, all patients were administered the recommended Phase 2 daratumumab dose (16 mg/kg), patients refractory to lenalidomide were excluded, and patients with at least one prior line of therapy were included.[2]

In this study, the most common adverse events (AEs) included neutropenia (84 percent), cough (47 percent), muscle spasms (44 percent) and diarrhoea (44 percent). Sixteen patients (50 percent) experienced serious AEs, but only neutropenia (n=3), gastroenteritis (n=2) and pyrexia (n=2) occurred in more than one patient. Eighteen patients (56 percent) had infusion reactions; these were generally mild to moderate (Grade ≤2) and usually occurred during the first infusion. Infusion reactions were managed with pre-medication or by slowing infusion rate. No additional safety signals were observed.[1]

Other Daratumumab Presentations at ASH

In a separate presentation researchers will present updated data from an ongoing open-label, multicentre, Phase 1b study showing daratumumab in combination with pomalidomide and dexamethasone produced rapid, deep and durable responses in relapsed or refractory multiple myeloma patients who had received at least two (median of 3.5) prior lines of therapy, including two or more consecutive cycles of lenalidomide and bortezomib, and were refractory to their last line of treatment. The combination of daratumumab with pomalidomide and dexamethasone was well-tolerated and resulted in little additional toxicity with the exception of daratumumab-related infusion reactions. The data will be presented during an oral abstract session on Monday, December 7 at 7:45 a.m. ET / 1:45 p.m. CET.[3]

Researchers also presented data from a combined efficacy analysis of the open-label, multicentre Phase 1/2 GEN501 and Phase 2 MMY2002 (SIRIUS) trials, which included heavily pre-treated patients with relapsed and refractory multiple myeloma who have exhausted other approved treatment options and whose disease was progressive at enrolment. After a median follow-up of 14.8 months, investigators estimated the median OS for single-agent daratumumab (16 mg/kg) would be 19.9 months (95 percent CI, 15.1–not estimable) for the combined analysis if patients continued treatment. A partial response or better was achieved by 31 percent of patients, and 83 percent achieved stable disease or better. These data were presented during an oral abstract session on Saturday, December 5.[4]

#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.[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] Across Europe, five-year survival rates are 23 percent to 47 percent of people diagnosed.[8] Almost 29 percent 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 which can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[7] Patients who relapse after treatment with standard therapies, including proteasome inhibitors (PIs) and immunomodulatory agents (IMiDs), have poor prognoses and few treatment options available.[10]

About Daratumumab

Daratumumab is a human CD38-directed monoclonal antibody which binds with high affinity to CD38, a surface protein that is over-expressed on most, if not all, multiple myeloma cells.[11] Daratumumab is believed to induce rapid tumour cell death through apoptosis, in which a series of molecular steps in a cell lead to its death[12,13] and multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).[12,14,15] 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 in which CD38 is expressed, such as smouldering myeloma and non-Hodgkin lymphoma. For more information, please see www.clinicaltrials.gov.

Daratumumab is currently under accelerated assessment by the European Medicines Agency. In the U.S., daratumumab is approved by the 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. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[12]

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-emea.com. Follow us on www.twitter.com/janssenEMEA for our latest news.

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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.

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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. 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 any of the Janssen Pharmaceutical Companies or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in new product development, including the uncertainty of clinical success and of obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; 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 December 28, 2014, 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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