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Darzalex®▼(daratumumab) Combination Regimen Significantly Improved Outcomes for Newly Diagnosed Multiple Myeloma Patients who are Transplant Ineligible

Phase 3 ALCYONE data for daratumumab in combination with bortezomib, melphalan and prednisone significantly improved progression-free survival and response rates

Data featured as late-breaker at ASH 2017 (Abstract #LBA-4) and published in the New England Journal of Medicine

BEERSE, BELGIUM, December 12, 2017 – Janssen-Cilag International NV ("Janssen") today announced data from the Phase 3 ALCYONE study, showing Darzalex® (daratumumab) in combination with bortezomib, melphalan and prednisone (VMP) significantly improved clinical outcomes, including reducing the risk of disease progression or death by 50 percent, in patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplantation (ASCT).[1] These data were accepted as a late-breaking abstract (LBA) for presentation at the 59th American Society of Hematology (ASH) Annual Meeting in Atlanta, today at 7:30 a.m. ET (Abstract #LBA-4).[1] Study findings were simultaneously published in the *New England Journal of Medicine (NEJM).*[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]

"These Phase 3 results for daratumumab demonstrated clinically meaningful improvements with a manageable safety profile," said Dr. Maria-Victoria Mateos, Ph.D., lead ALCYONE study investigator and Director of the Myeloma Unit at University Hospital of Salamanca-IBSAL Salamanca, Spain. "Selecting the right treatment regimen is critical for patients who are newly diagnosed, especially if they are transplant ineligible, as these patients tend to be older and more frail. These findings strongly support this daratumumab frontline regimen as a new standard of care for transplant-ineligible newly diagnosed patients with multiple myeloma."

At a median follow-up of 16.5 months, daratumumab-VMP reduced the risk of disease progression or death by 50 percent, compared to treatment with VMP alone (Hazard Ratio [HR] = 0.50; 95 percent CI [0.38-0.65], p<0.0001).[1] The median progression free survival (PFS) for daratumumab-VMP had not yet been reached, compared to an estimated median PFS of 18.1 months for patients who received VMP alone.[1]

In addition to reducing the risk of disease progression or death, daratumumab significantly improved the overall response rate (ORR) (90.9 percent vs. 73.9 percent) compared to VMP alone, including more than doubling rates of stringent complete response (sCR) (18 percent vs. 7 percent) and significantly improving rates of very good partial response (VGPR) or better (71 percent vs. 50 percent) and complete response (CR) or better (43 percent vs. 24 percent).[1] Patients receiving daratumumab also reported a more than three-fold increase in the minimal residual disease (MRD) negativity rate (22 percent vs. 6 percent) compared to those who received VMP alone.[1]

The most common (≥10 percent) Grade 3/4 treatment emergent adverse events (TEAEs) were neutropenia (40 percent vs. 39 percent), thrombocytopenia (34 percent vs. 38 percent), anaemia (16 percent vs. 20 percent) and pneumonia (11 percent vs. 4 percent).[1] One patient in each arm discontinued treatment due to pneumonia and 0.9 percent of patients discontinued daratumumab due to an infection.[1,4] Twenty-eight percent of patients experienced IRRs due to daratumumab, and most IRRs occurred during the first infusion.[1,4] In the daratumumab-VMP arm, 42 percent of patients experienced a serious adverse event (SAE), compared to 33 percent in the VMP arm. The most common (≥2 percent) SAEs (daratumumab-VMP vs. VMP) were pneumonia (10 percent vs. 3 percent), anaemia (2 percent vs. 3 percent), bronchitis (2 percent vs. 1 percent), upper respiratory tract infection

(2 percent vs. 1 percent), cardiac failure (<1 percent vs. 2 percent) and febrile neutropenia (1 percent vs. 2 percent).[4]

"This is the third Phase 3 study in which daratumumab has demonstrated a consistent doubling of progression free survival when combined with standard regimens,'" said Dr Catherine Taylor, Haematology Therapeutic Area Lead, Janssen Europe, Middle East and Africa (EMEA). "The ALCYONE study results showed the clinical benefit daratumumab offers to treatment naïve patients in the non-transplant setting."

On November 21, 2017, Janssen submitted an application to the European Medicines Agency (EMA) seeking to expand the existing marketing authorisation for daratumumab in combination with VMP for this patient population.[5] If approved, this would be the first indication for daratumumab in the frontline setting.

On November 21, 2017, Janssen also submitted a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) for daratumumab in this patient population. Janssen requested Priority Review of this sBLA, which would shorten FDA review to six months, compared to ten months for Standard Review. If approved, this would be the fifth indication for daratumumab in the U.S.[6]

#ENDS#

About the ALCYONE Trial[1]

The randomised, open-label, multicentre Phase 3 ALCYONE (MMY3007) study enrolled 706 newly diagnosed patients with multiple myeloma who were ineligible for high-dose chemotherapy with ASCT. In the daratumumab-VMP arm, the median (range) age was 71 (40-93) years; 30 percent were ≥75 years and 46 percent were male.[1] Patients were randomised to receive nine cycles of either daratumumab combined with VMP, or VMP alone.[1] In the daratumumab-VMP arm, patients received 16 mg/kg of daratumumab once weekly for six weeks (cycle 1; 1 cycle = 42 days), followed by once every three weeks (cycles 2-9). Following the nine cycles, patients in the daratumumab-VMP arm continued to receive 16 mg/kg of daratumumab once every four weeks until disease progression.[1]

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.[7,8,9] 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.[10-18] 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 the potential of daratumumab and expectations for its further 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 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; 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. 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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