



NEWS RELEASE

First Phase 3 Trial of Daratumumab in Combination with Standard Therapy in Relapsed/Refractory Multiple Myeloma Meets Primary Endpoint in Planned Interim Analysis

3/30/2016

First Phase 3 Trial of Daratumumab in Combination with Standard Therapy in Relapsed/Refractory Multiple Myeloma Meets Primary Endpoint in Planned Interim Analysis

RARITAN, N.J., March 30, 2016 /PRNewswire/ -- Janssen Research & Development, LLC announced today positive results of a pre-planned interim analysis of the Phase 3 MMY3004 (CASTOR) trial evaluating the efficacy and safety of daratumumab, a CD38-directed monoclonal antibody (mAb), in combination with bortezomib and dexamethasone, compared to bortezomib and dexamethasone alone, in patients with relapsed or refractory multiple myeloma. The interim analysis, conducted by an Independent Data Monitoring Committee (IDMC), found that the daratumumab combination treatment regimen improved progression-free survival (PFS) compared with bortezomib and dexamethasone alone, achieving the primary study endpoint ($p < 0.0001$). Based on the recommendation of the IDMC, the study will be stopped early. Study patients originally assigned to the standard treatment group (bortezomib plus dexamethasone) will be offered the option of receiving daratumumab following confirmed disease progression. All patients continue to be followed for long-term safety and overall survival.

"These results suggest daratumumab could potentially be used in combination with standard therapy in patients with relapsed or refractory multiple myeloma," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Head, Janssen Research & Development. "We are especially proud that Janssen was involved in the development of two of the medicines in this trial, daratumumab and bortezomib." Janssen licensed daratumumab from Genmab A/S and is responsible for development and marketing. Janssen co-developed bortezomib with Takeda Pharmaceutical Company Limited through its wholly owned subsidiary Millennium Pharmaceuticals Inc. and commercializes the

treatment outside of the U.S.

MMY3004 is a Phase 3, multinational, open-label, randomized, multicenter, active-controlled study in approximately 490 patients with relapsed or refractory multiple myeloma. Patients were randomized to receive either daratumumab combined with subcutaneous bortezomib (a proteasome inhibitor) and dexamethasone (a corticosteroid), or bortezomib and dexamethasone alone. Participants were treated until disease progression, unacceptable toxicity, or if they had other reasons to discontinue the study. The primary endpoint of the study is PFS.¹

These results are planned to be submitted for presentation at an upcoming medical congress, as well as for publication in a peer-reviewed journal. A full study report is being prepared for submission and will be shared with health authorities. Janssen will initiate discussions about the potential for a regulatory submission for this indication. For additional study information, visit [ClinicalTrials.gov](https://clinicaltrials.gov).

In **November 2015**, daratumumab (DARZALEX[®]) was approved by the U.S. Food and Drug Administration for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent, or who are double-refractory to a PI and an immunomodulatory agent. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.²

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow.^{3,4} Refractory cancer occurs when a patient's disease is resistant to treatment or in the case of multiple myeloma, the disease progresses within 60 days of their last therapy.^{5,6} Relapsed cancer means the disease has returned after a period of initial, partial or complete remission.⁵ Accounting for approximately one percent of all cancers and 15 percent to 20 percent of haematologic malignancies worldwide, multiple myeloma is designated as an orphan disease in both the U.S. and Europe.⁷ Globally, it is estimated that 124,225 people were diagnosed, and 87,084 died from the disease in 2015.^{8,9} While some patients with multiple myeloma 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.¹⁰ Patients who relapse after treatment with standard therapies (including PIs or immunomodulatory agents) typically have poor prognoses and few remaining options.⁴

About DARZALEX[®] (daratumumab)

DARZALEX[®] (daratumumab) injection for intravenous use is the first CD38-directed monoclonal antibody (mAb) approved anywhere in the world.² CD38 is a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.¹¹ Daratumumab is believed to induce tumor cell death through apoptosis, in which a

series of molecular steps in a cell lead to its death^{2,12} as well as immunomodulatory effects and multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).^{2,13,14} 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, such as smoldering myeloma and non-Hodgkin's lymphoma. DARZALEX is the first mAb to receive regulatory approval to treat relapsed or refractory multiple myeloma.²

In **August 2012**, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize DARZALEX. DARZALEX is commercialized in the U.S. by Janssen Biotech, Inc.¹⁵

DARZALEX® (daratumumab) Important Safety Information - Professional

CONTRAINDICATIONS - None

WARNINGS AND PRECAUTIONS

Infusion Reactions - DARZALEX can cause severe infusion reactions. Approximately half of all patients experienced a reaction, most during the first infusion. Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing an infusion. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, and hypertension. Signs and symptoms may include respiratory symptoms, such as cough, wheezing, larynx and throat tightness and irritation, laryngeal edema, pulmonary edema, nasal congestion, and allergic rhinitis. Less common symptoms were hypotension, headache, rash, urticaria, pruritus, nausea, vomiting, and chills.

Pre-medicate patients with antihistamines, antipyretics and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt infusion for reactions of any severity and institute medical management as needed. Permanently discontinue therapy for life-threatening (Grade 4) reactions. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients the first and second day after all infusions. Patients with a history of obstructive pulmonary disorders may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with obstructive pulmonary disorders.

Interference with Serological Testing - Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX. Type and screen patients prior to starting DARZALEX.

Interference with Determination of Complete Response - Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both, the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Adverse Reactions - The most frequently reported adverse reactions (incidence =20%) were: fatigue, nausea, back pain, pyrexia, cough, and upper respiratory tract infection.

Serious adverse reactions were reported in 51 (33%) patients. The most frequent serious adverse reactions were pneumonia (6%), general physical health deterioration (3%), and pyrexia (3%).

DRUG INTERACTIONS - No drug interaction studies have been performed.

About Janssen Research & Development, LLC

At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Janssen Research & Development, LLC; and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Please visit www.janssen.com for more information.

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 hematologic 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, individualized use of our therapies; as well as safe and effective identification and treatment of early changes in the tumor microenvironment. Please visit <http://www.janssen.com> for more information.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding a clinical trial collaboration and 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 Janssen Research & Development, LLC and/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 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.

¹ ClinicalTrials.gov. Addition of Daratumumab to Combination of Bortezomib and Dexamethasone in Participants With Relapsed or Refractory Multiple Myeloma. Available at <https://clinicaltrials.gov/ct2/show/NCT02136134>. Accessed March 2016.

² DARZALEX Prescribing Information, November 2015. Available at <https://www.darzalex.com/shared/product/darzalex/darzalex-prescribing-information.pdf>. Accessed March 2016.

³ American Cancer Society. "Multiple Myeloma Overview." <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma>. Accessed March 2016.

⁴ Kumar, SK et al. Leukemia. 2012 Jan; 26(1):149-57.

⁵ National Cancer Institute. "NCI Dictionary of Cancer Terms: Refractory." Available at <http://www.cancer.gov/publications/dictionaries/cancer-terms?expand=R>. Accessed March 2016.

⁶ Richardson, et al. "The Treatment of Relapsed and Refractory Multiple Myeloma." ASH Education Book January 1, 2007 vol. 2007 no. 1 317-323.

⁷ Becker N. Epidemiology of multiple myeloma. Recent results in cancer research. Fortschritte der Krebsforschung. Progres dans les recherches sur le cancer. 2011;183:25-35.

⁸ GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide: Number of New Cancers in 2015. Available at http://globocan.iarc.fr/old/burden.asp?selection_pop=224900&Text-p=World&selection_cancer=17270&Text-c=Multiple+myeloma&pYear=3&type=0&window=1&submit=%C2%A0Execute. Accessed March 2016.

⁹ GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide: Number of Cancer Deaths in 2015. Available at http://globocan.iarc.fr/old/burden.asp?selection_pop=224900&Text-p=World&selection_cancer=17270&Text-c=Multiple+myeloma&pYear=3&type=1&window=1&submit=%C2%A0Execute. Accessed March 2016.

¹⁰ American Cancer Society. "How is Multiple Myeloma Diagnosed?" <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-diagnosis>. Accessed March 2016.

¹¹ Fedele, G et al. CD38 Ligation in Peripheral Blood Mononuclear Cells of Myeloma Patients Induces Release of Protumorigenic IL-6 and Impaired Secretion of IFN γ Cytokines and Proliferation. Mediators Inflamm. 2013;2013:564687.

¹² Jansen, JH et al. Blood. 2012; 120:2974.

¹³ de Weers, M et al. Daratumumab, a Novel Therapeutic Human CD38 Monoclonal Antibody, Induces Killing of Multiple Myeloma and Other Hematological Tumors. The Journal of Immunology. February 1, 2011. Vol. 186, No. 3 1840-1848.

¹⁴ Overdijk, M et al. Phagocytosis Is A Mechanism of Action for Daratumumab. Available at <https://ash.confex.com/ash/2012/webprogram/Paper51257.html>. Accessed March 2016.

¹⁵ Janssen Biotech, Inc. "Janssen Biotech Announces Global License and Development Agreement for Investigational Anti-Cancer Agent Daratumumab." Issued August 30, 2012.

Media Inquiries:

Kellie McLaughlin

Phone: 1-908-927-7477

Mobile: 1-609-468-8356

Satu Kaarina Glawe

Mobile: +49 172 294 62 64

Investor Relations:

Lesley Fishman

Phone: 1-732-524-3922

Louise Mehrotra

Phone: 1-732-524-6491

U.S. Medical Inquiries:

1-800-526-7736