



NEWS RELEASE

# DARZALEX® (daratumumab) Approved by U.S. FDA: First Human Anti-CD38 Monoclonal Antibody Available for the Treatment of Multiple Myeloma

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HORSHAM, PA, November 16, 2015 - Janssen Biotech, Inc., a Janssen Pharmaceutical Company of Johnson & Johnson, announced today the U.S. Food and Drug Administration (FDA) has approved DARZALEX® (daratumumab) injection for intravenous infusion 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<sup>1</sup>. 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. Multiple myeloma is an incurable blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow.<sup>2,3</sup> 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.<sup>4,5</sup> Relapsed cancer means the disease has returned after a period of initial, partial or complete remission.<sup>6</sup>

DARZALEX is the first human anti-CD38 monoclonal antibody (mAb) approved anywhere in the world. CD38 is a surface protein that is expressed by most, if not all, multiple myeloma cells.<sup>7</sup> DARZALEX is believed to induce tumor cell death through multiple immune-mediated mechanisms of action,<sup>8,9</sup> in addition to apoptosis, in which a series of molecular steps in a cell lead to its death.<sup>10</sup> Its approval comes just two months after the Biologics License Application (BLA) was accepted for Priority Review by the FDA in **September 2015**.<sup>11</sup> DARZALEX received Breakthrough Therapy Designation from the FDA for this indication in **May 2013**.<sup>12</sup>

"Multiple myeloma is a highly complex disease and remains incurable, with almost all patients relapsing or



becoming resistant to therapy," said DARZALEX clinical trial investigator Paul G. Richardson, M.D., Clinical Program Leader and Director of Clinical Research, Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute. "With DARZALEX, we have a promising new immunotherapy, which has shown pronounced efficacy as a single agent with an acceptable adverse event profile. This is especially important for treating these heavily pre-treated patients in whom all of the major classes of currently available medicines have failed."

The pivotal open-label Phase 2 MMY2002 (SIRIUS) study showed treatment with single-agent DARZALEX resulted in an overall response rate (ORR) of 29.2 percent (95% CI; 20.8, 38.9) in patients who received a median of five prior lines of therapy, including a PI and an immunomodulatory agent.<sup>1</sup> Stringent complete response (sCR) was reported in 2.8 percent of patients, very good partial response (VGPR) was reported in 9.4 percent of patients, and partial response (PR) was reported in 17 percent of patients.<sup>1</sup> These efficacy results were based on ORR as determined by the Independent Review Committee assessment using IMWG (International Myeloma Working Group) criteria and the range for median duration of response.

For responders, the median duration of response was 7.4 months (range 1.2-13.1+ months).<sup>1</sup> At baseline, 97 percent of patients were refractory to their last line of therapy, 95 percent were refractory to both a PI and an immunomodulatory agent, and 77 percent were refractory to alkylating agents.<sup>1</sup> Additional efficacy data from the Phase 1/2 GEN501 monotherapy study - published in *The New England Journal of Medicine* in **August 2015** - also support this approval.<sup>1</sup>

"The responses we saw in clinical trials that led to today's approval were striking, especially considering that these patients received a median of five prior lines of therapy," said MMY2002 investigator Sagar Lonial, M.D., Chief Medical Officer, Winship Cancer Institute of Emory University and Professor and Executive Vice Chair, Department of Hematology and Medical Oncology, Emory University School of Medicine. "It appears the mechanism of action for daratumumab (DARZALEX) may play an important role in its single-agent activity among this group of advanced-stage multiple myeloma patients."

"Living with multiple myeloma is challenging, both physically and emotionally, especially as the disease progresses and treatment options become more limited," said Debby Graff, a patient enrolled in a clinical trial at Dana-Farber Cancer Institute. "I am encouraged by emerging treatments for multiple myeloma, and I have a new outlook on my path forward."

"While there have been considerable improvements over the past decade in the treatment of people living with multiple myeloma, these patients face a long, hard road - especially those whose disease has relapsed or is no longer responding to current therapies," said Walter M. Capone, President and Chief Executive Officer of the Multiple Myeloma Research Foundation (MMRF). "With the approval of daratumumab, a new antibody option targeting CD38, along with ongoing work to advance the development of novel classes of therapies by both Janssen

and MMRF, we are ushering in a new era of myeloma therapy focused on individualized treatment approaches for patients with significant unmet needs."

"Our focus is developing transformational medicines for people living with hard-to-treat cancers, such as multiple myeloma," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Head, Janssen. "The rapid development and approval of DARZALEX - the first human anti-CD38 monoclonal antibody - is a great example of this commitment and our ongoing work in developing immunotherapies. We will continue to study this compound as both a mono- and a combination therapy to understand its full clinical benefit for patients across the treatment continuum in multiple myeloma and other tumor types."

The warnings and precautions for DARZALEX include infusion reactions, interference with serological testing and interference with determination of complete response (see Important Safety Information).<sup>1</sup> The most frequently reported adverse reactions (incidence  $\geq 20\%$ ) were: fatigue, nausea, back pain, pyrexia, cough and upper respiratory tract infection.<sup>1</sup>

In data from three pooled clinical studies including a total of 156 patients, four percent of patients discontinued treatment due to adverse reactions.<sup>1</sup> Infusion reactions were reported in approximately half of all patients treated with DARZALEX.<sup>1</sup> Common ( $\geq 5$  percent) symptoms of infusion reactions included nasal congestion, chills, cough, allergic rhinitis, throat irritation, dyspnea (shortness of breath) and nausea.<sup>1</sup> Severe infusion reactions, including bronchospasm, dyspnea, hypoxia and hypertension ( $< 2$  percent each).<sup>1</sup>

The recommended dose of DARZALEX is 16 mg/kg body weight administered as an intravenous infusion.<sup>1</sup> The dosing schedule begins with weekly administration (weeks 1-8) and reduces in frequency over time to every two weeks (weeks 9-24) and ultimately every four weeks (week 25 onwards until disease progression).<sup>1</sup>

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.<sup>13</sup> Janssen is currently the global sponsor of all but one clinical study. DARZALEX will be commercialized in the U.S. by Janssen Biotech, Inc.

## About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow.<sup>2,3</sup> Multiple myeloma is the third most common blood cancer in the U.S., following only leukemia and lymphoma.<sup>14</sup> Approximately 26,850 new patients will be diagnosed with multiple myeloma, and approximately 11,240 people will die from the disease in the U.S. in 2015.<sup>15</sup> Globally, it is estimated that 124,225 people will be diagnosed, and 87,084 will die from the disease in 2015.<sup>16,17</sup> 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.<sup>18</sup> Patients who relapse after treatment with standard

therapies (including PIs or immunomodulatory agents) typically have poor prognoses and few remaining options.<sup>3</sup>

### **Access to DARZALEX® (daratumumab) Injection, for Intravenous Infusion**

DARZALEX (daratumumab) injection for intravenous infusion will be available for distribution in the U.S. within two weeks following FDA approval. Janssen Biotech offers comprehensive access and support information, resources and services to assist U.S. patients in gaining access to DARZALEX through the Janssen CarePath Program. For more information, health care providers or patients can contact: 1-844-55DARZA (1-844-553-2792). Information will also be available at [www.DARZALEX.com](http://www.DARZALEX.com). Dedicated case coordinators are available to work with both healthcare providers and patients.

Patients with private or commercial insurance may be eligible for the Janssen CarePath Savings Program for DARZALEX. Information on the enrollment process will be available online at [www.CarePathSavingsProgram.com/DARZALEX](http://www.CarePathSavingsProgram.com/DARZALEX).

### **About DARZALEX® (daratumumab) Injection, for Intravenous Infusion**

DARZALEX® (daratumumab) injection for intravenous infusion is indicated 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.<sup>1</sup> 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. DARZALEX is the first human anti-CD38 monoclonal antibody (mAb) to receive U.S. Food and Drug Administration (FDA) approval to treat multiple myeloma. DARZALEX is believed to induce tumor cell death through apoptosis, in which a series of molecular steps in a cell lead to its death<sup>1,10</sup> and multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).<sup>1,8</sup> More information will be available at [www.DARZALEX.com](http://www.DARZALEX.com).

### **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  $\geq 20\%$ ) were: fatigue, nausea, back pain, pyrexia, cough, and upper respiratory tract infection.

Serious adverse reactions were reported in 51 (33%) of 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 Biotech, Inc.

Janssen Biotech, Inc. redefines the standard of care in immunology, oncology, urology and nephrology. Built upon a rich legacy of innovative firsts, Janssen Biotech has delivered on the promise of new treatments and ways to improve the health of individuals with serious disease. Beyond its innovative medicines, Janssen Biotech is at the forefront of developing education and public policy initiatives to ensure patients and their families, caregivers,

advocates and health care professionals have access to the latest treatment information, support services and quality care. For more information on Janssen Biotech, Inc. or its products, visit [www.janssenbiotech.com](http://www.janssenbiotech.com). Follow us on Twitter at [www.twitter.com/JanssenUS](http://www.twitter.com/JanssenUS).

## Janssen in Oncology

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 [oncology.janssenrnd.com](http://oncology.janssenrnd.com).

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 Janssen Biotech, Inc. 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 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](http://www.sec.gov), [www.jnj.com](http://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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<sup>1</sup> DARZALEX Prescribing Information, November 2015.

<sup>2</sup> American Cancer Society. "Multiple Myeloma Overview."  
<http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma>. Accessed November 2015.

<sup>3</sup> Kumar, SK et al. Leukemia. 2012 Jan; 26(1):149-57.

<sup>4</sup> National Cancer Institute. "NCI Dictionary of Cancer Terms: Refractory." Available at

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- <sup>5</sup> Richardson, et al. "The Treatment of Relapsed and Refractory Multiple Myeloma." ASH Education Book January 1, 2007 vol. 2007 no. 1 317-323.
- <sup>6</sup> National Cancer Institute. "NCI Dictionary of Cancer Terms: Relapsed." Available at <http://www.cancer.gov/publications/dictionaries/cancer-terms?expand=R>. Accessed November 2015.
- <sup>7</sup> 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 $\gamma$  Cytokines and Proliferation. *Mediators Inflamm.* 2013;2013:564687.
- <sup>8</sup> Michel de Weers 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.
- <sup>9</sup> Overdijk et al. Phagocytosis Is A Mechanism of Action for Daratumumab. Available at <https://ash.confex.com/ash/2012/webprogram/Paper51257.html>. Accessed September 2015.
- <sup>10</sup> Jansen JH, et al. *Blood.* 2012; 120:2974.
- <sup>11</sup> Janssen Research & Development, LLC. "U.S. FDA Grants Priority Review to Janssen for Daratumumab as a Treatment for Multiple Myeloma." Issued September 4, 2015.
- <sup>12</sup> Janssen Research & Development, LLC. "Daratumumab Receives Breakthrough Therapy Designation in Double Refractory Multiple Myeloma from U.S. Food and Drug Administration." Issued May 1, 2013.
- <sup>13</sup> Janssen Biotech, Inc. "Janssen Biotech Announces Global License and Development Agreement for Investigational Anti-Cancer Agent Daratumumab." Issued August 30, 2012.
- <sup>14</sup> National Cancer Institute. "A Snapshot of Myeloma." Available at [www.cancer.gov/research/progress/snapshots/myeloma](http://www.cancer.gov/research/progress/snapshots/myeloma). Accessed November 2015.
- <sup>15</sup> American Cancer Society. "What are the key statistics about multiple myeloma?" <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-key-statistics>. Accessed November 2015.
- <sup>16</sup> 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](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 November 2015.
- <sup>17</sup> 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](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 November 2015.
- <sup>18</sup> American Cancer Society. "How is Multiple Myeloma Diagnosed?" <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-diagnosis>. Accessed

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