

## **U.S. FDA Grants Priority Review for Daratumumab in Combination with Bortezomib, Thalidomide and Dexamethasone in Frontline Multiple Myeloma**

### **Company Announcement**

- **U.S. FDA grants Priority Review for daratumumab in combination with bortezomib, thalidomide and dexamethasone as treatment for newly diagnosed patients with multiple myeloma who are candidates for autologous stem cell transplant**
- **September 26, 2019 PDUFA date**

**Copenhagen, Denmark; May 30, 2019 – Genmab A/S (Nasdaq Copenhagen: GEN) announced today that the U.S. Food and Drug Administration (U.S. FDA) granted a Priority Review for the supplemental Biologics License Application (sBLA) for the use of daratumumab (DARZALEX®) in combination with bortezomib, thalidomide and dexamethasone (VTd) as treatment for patients newly diagnosed with multiple myeloma who are candidates for autologous stem cell transplant (ASCT).** The sBLA was submitted by Genmab's licensing partner, Janssen Biotech, Inc. (Janssen), in March 2019. Priority Review is a U.S. FDA designation for drugs that treat a serious condition and may provide a significant improvement in safety or efficacy. The U.S. FDA assigned a Prescription Drug User Fee Act (PDUFA) target date of September 26, 2019 to take a decision on daratumumab in this indication. In August 2012, Genmab granted Janssen an exclusive worldwide license to develop, manufacture and commercialize daratumumab.

The sBLA submission is based on data from the Phase III CASSIOPEIA study of daratumumab in combination with VTd as treatment for patients newly diagnosed with multiple myeloma who are candidates for ASCT. The study is sponsored by the French Intergroupe Francophone du Myelome (IFM) in collaboration with the Dutch-Belgian Cooperative Trial Group for Hematology Oncology (HOVON) and Janssen. Genmab announced topline results from the trial in October 2018 and the American Society of Clinical Oncology (ASCO) accepted an abstract containing more complete data, submitted by Janssen, for oral presentation at the 2019 ASCO Annual meeting in June 2019.

“Thanks to the strong collaborative effort of IFM, HOVON and Janssen, should the U.S. FDA approve this sBLA, patients in the United States newly diagnosed with multiple myeloma who are eligible candidates for ASCT may one day also be able to include DARZALEX in combination with VTd in their treatment regimen,” said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

### **About the CASSIOPEIA (MMY3006) study**

This Phase III study is a randomized, open-label, multicenter study, run by the French Intergroupe Francophone du Myelome (IFM) in collaboration with the Dutch-Belgian Cooperative Trial Group for Hematology Oncology (HOVON) and Janssen, including 1,085 newly diagnosed patients with previously untreated symptomatic multiple myeloma who are eligible for high dose chemotherapy and stem cell transplant. In the first part of the study, patients were randomized to receive induction and consolidation treatment with daratumumab combined with bortezomib, thalidomide (an immunomodulatory agent) and dexamethasone (a corticosteroid) or bortezomib, thalidomide and dexamethasone alone. The primary endpoint is the proportion of patients that achieve a stringent Complete Response (sCR). In the second part of the study, patients that achieved a response will undergo a second randomization to either receive maintenance treatment of daratumumab 16 mg/kg every 8 weeks for up to 2 years versus no further treatment (observation). The primary endpoint of this part of the study is progression free survival (PFS).

### **About multiple myeloma**

Multiple myeloma is an incurable blood cancer that starts in the bone marrow and is characterized by an excess proliferation of plasma cells.<sup>1</sup> Multiple myeloma is the third most common blood cancer in the U.S., after leukemia and lymphoma.<sup>2</sup> Approximately 26,000 new patients were expected to be diagnosed with multiple myeloma and approximately 13,650 people were expected to die from the disease in the U.S. in 2018.<sup>3</sup> Globally, it was estimated that 160,000 people were diagnosed and 106,000 died from the

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disease in 2018.<sup>4</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>5</sup>

### About DARZALEX® (daratumumab)

DARZALEX® (daratumumab) intravenous infusion is indicated in the United States in combination with bortezomib, melphalan and prednisone for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant; in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy; in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor (PI); and as a monotherapy 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.<sup>6</sup> DARZALEX is the first monoclonal antibody (mAb) to receive U.S. Food and Drug Administration (U.S. FDA) approval to treat multiple myeloma. DARZALEX is indicated in Europe in combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant; 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; and as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a PI and an immunomodulatory agent and who have demonstrated disease progression on the last therapy. The option to split the first infusion of DARZALEX over two consecutive days has been approved in both Europe and the U.S. In Japan, DARZALEX is approved in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adults with relapsed or refractory multiple myeloma. DARZALEX is the first human CD38 monoclonal antibody to reach the market in the United States, Europe and Japan. For more information, visit [www.DARZALEX.com](http://www.DARZALEX.com).

Daratumumab is a human IgG1k monoclonal antibody (mAb) that binds with high affinity to the CD38 molecule, which is highly expressed on the surface of multiple myeloma cells. Daratumumab triggers a person's own immune system to attack the cancer cells, resulting in rapid tumor cell death through multiple immune-mediated mechanisms of action and through immunomodulatory effects, in addition to direct tumor cell death, via apoptosis (programmed cell death).<sup>6,7,8,9,10</sup>

Daratumumab is being developed by Janssen Biotech, Inc. under an exclusive worldwide license to develop, manufacture and commercialize daratumumab from Genmab. A comprehensive clinical development program for daratumumab is ongoing, including multiple Phase III studies in smoldering, relapsed and frontline multiple myeloma settings and in amyloidosis. Additional studies are ongoing or planned to assess the potential of daratumumab in other malignant and pre-malignant diseases, such as NKT-cell lymphoma, B and T-ALL. Daratumumab has received two Breakthrough Therapy Designations

### About Genmab

Genmab is a publicly traded, international biotechnology company specializing in the creation and development of differentiated antibody therapeutics for the treatment of cancer. Founded in 1999, the company has two approved antibodies, DARZALEX® (daratumumab) for the treatment of certain multiple myeloma indications, and Arzerra® (ofatumumab) for the treatment of certain chronic lymphocytic leukemia indications. Daratumumab is in clinical development for additional multiple myeloma indications, other blood cancers and amyloidosis. A subcutaneous formulation of ofatumumab is in development for relapsing multiple sclerosis. Genmab also has a broad clinical and pre-clinical product pipeline. Genmab's technology base consists of validated and proprietary next generation antibody technologies - the DuoBody® platform for generation of bispecific antibodies, the HexaBody® platform, which creates effector function enhanced antibodies and the HexElect® platform, which combines two co-

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independently acting HexaBody molecules to introduce selectivity while maximizing therapeutic potency. The company intends to leverage these technologies to create opportunities for full or co-ownership of future products. Genmab has alliances with top tier pharmaceutical and biotechnology companies. For more information visit [www.genmab.com](http://www.genmab.com).

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Genmab A/S and/or its subsidiaries own the following trademarks: Genmab<sup>®</sup>; the Y-shaped Genmab logo<sup>®</sup>; Genmab in combination with the Y-shaped Genmab logo<sup>®</sup>; HuMax<sup>®</sup>; DuoBody<sup>®</sup>; DuoBody in combination with the DuoBody logo<sup>®</sup>; HexaBody<sup>®</sup>; HexaBody in combination with the HexaBody logo<sup>®</sup>; DuoHexaBody<sup>®</sup>; HexElect<sup>®</sup>; and UniBody<sup>®</sup>. Arzerra<sup>®</sup> is a trademark of Novartis AG or its affiliates. DARZALEX<sup>®</sup> is a trademark of Janssen Pharmaceutica NV.

<sup>1</sup> American Cancer Society. "Multiple Myeloma Overview." Available at <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma>. Accessed June 2016.

<sup>2</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 June 2016.

<sup>3</sup> Globocan 2018. United States of America Fact Sheet. Available at <http://gco.iarc.fr/today/data/factsheets/840-united-states-of-america-fact-sheets.pdf>.

<sup>4</sup> Globocan 2018. World Fact Sheet. Available at <http://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf>. Accessed December 2018.

<sup>5</sup> American Cancer Society. "How is Multiple Myeloma Diagnosed?" <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-diagnosis>. Accessed June 2016.

<sup>6</sup> DARZALEX Prescribing information, February 2019. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/761036s016lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761036s016lbl.pdf) Last accessed February 2019

<sup>7</sup> 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*. 2011; 186: 1840-1848.

<sup>8</sup> Overdijk, MB, et al. Antibody-mediated phagocytosis contributes to the anti-tumor activity of the therapeutic antibody daratumumab in lymphoma and multiple myeloma. *MAbs*. 2015; 7: 311-21.

<sup>9</sup> Krejci, MD et al. Daratumumab Depletes CD38+ Immune-regulatory Cells, Promotes T-cell Expansion, and Skews T-cell Repertoire in Multiple Myeloma. *Blood*. 2016; 128: 384-94.

<sup>10</sup> Jansen, JH et al. Daratumumab, a human CD38 antibody induces apoptosis of myeloma tumor cells via Fc receptor-mediated crosslinking. *Blood*. 2012; 120(21): abstract 2974.