

## **Genmab Announces U.S. FDA Approval of DARZALEX® (daratumumab) in Combination with Lenalidomide and Dexamethasone in Frontline Multiple Myeloma**

### **Company Announcement**

- **DARZALEX (daratumumab) approved by U.S. FDA in combination with lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant**
- **Approval based on Phase III MAIA study**

**Copenhagen, Denmark; June 27, 2019 – Genmab A/S (Nasdaq Copenhagen: GEN) announced today that the U.S. Food and Drug Administration (U.S. FDA) has approved the use of DARZALEX® (daratumumab) in combination with lenalidomide and dexamethasone (Rd) for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).** The supplemental Biologics License Application (sBLA) for this indication was submitted by Genmab's licensing partner, Janssen Biotech, Inc., under the Real-Time Oncology Review (RTOR) pilot program. In August 2012, Genmab granted Janssen Biotech, Inc. an exclusive worldwide license to develop, manufacture and commercialize daratumumab.

"The combination of lenalidomide and dexamethasone is broadly used by newly diagnosed patients with multiple myeloma ineligible for ASCT in the United States. We are extremely pleased that physicians can now offer their patients the option to add DARZALEX to this regimen in the U.S.," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

The approval was based on data from the Phase III MAIA (MMY3008) study of daratumumab in combination with lenalidomide and dexamethasone as treatment for patients with newly diagnosed multiple myeloma, who are not candidates for high dose chemotherapy and ASCT. Data from this study was presented as a Late-Breaking Abstract at the 2018 American Society of Hematology (ASH) Annual Meeting in December 2018.

#### **About the MAIA (MMY3008) study**

The Phase III study (NCT02252172) is a randomized, open-label, multicenter study that includes 737 newly diagnosed patients with multiple myeloma who are not candidates for high dose chemotherapy and ASCT. Patients were randomized to receive either daratumumab in combination with lenalidomide (an immunomodulatory drug) and dexamethasone (a corticosteroid) or lenalidomide and dexamethasone alone. In the daratumumab treatment arm, patients received 16 milligrams per kilogram (mg/kg) weekly for first 8 weeks (Cycles 1 and 2), every other week for 16 weeks (Cycles 3 to 6) and then every 4 weeks (Cycle 7 and beyond) until progression of disease or unacceptable toxicity. Lenalidomide was administered at 25 mg orally on days 1 through 21 of each 28-day cycle, and dexamethasone was administered at 40 mg once a week for both treatment arms. Participants in both treatment arms will continue treatment with lenalidomide and dexamethasone until disease progression or unacceptable toxicity. The primary endpoint of the study is progression free survival.

#### **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 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>

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### About DARZALEX<sup>®</sup> (daratumumab)

DARZALEX<sup>®</sup> (daratumumab) intravenous infusion is indicated in the United States in combination with lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant; 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 from the U.S. FDA, for multiple myeloma, as both a monotherapy and in combination with other therapies.

### 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<sup>®</sup> (daratumumab) for the treatment of certain multiple myeloma indications, and Arzerra<sup>®</sup> (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<sup>®</sup> platform for generation of bispecific antibodies, the HexaBody<sup>®</sup> platform, which creates effector

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function enhanced antibodies and the HexElect<sup>®</sup> platform, which combines two co-dependently 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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<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> Krejcik, 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.