

## **Genmab Announces European Marketing Authorization for DARZALEX® (Daratumumab) in Combination with Lenalidomide and Dexamethasone in Frontline Multiple Myeloma**

### **Company Announcement**

- **DARZALEX® approved in Europe in combination with lenalidomide and dexamethasone as treatment for adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant**
- **Approval follows positive opinion by European Committee for Medicinal Products for Human Use (CHMP) in October**
- **Approval based on data from Phase III MAIA study**

**Copenhagen, Denmark; November 19, 2019 – Genmab A/S (Nasdaq: GMAB) announced today that the European Commission (EC) has granted marketing authorization for DARZALEX® (daratumumab) in combination with lenalidomide and dexamethasone (Rd) as treatment for adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).** The EC approval follows a positive opinion issued for DARZALEX by the CHMP of the European Medicines Agency (EMA) in October 2019. In August 2012, Genmab granted Janssen Biotech, Inc. (Janssen) an exclusive worldwide license to develop, manufacture and commercialize daratumumab.

“We are pleased that with this approval, patients in the European Union newly diagnosed with multiple myeloma who are not candidates for transplant will now have two potential options for treatment with DARZALEX containing regimens. We look forward to seeing the combination therapy of DARZALEX with lenalidomide and dexamethasone launched in Europe,” 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 Rd as treatment for patients with newly diagnosed multiple myeloma, who are not candidates for high dose chemotherapy and ASCT. Data from this study was published in *The New England Journal of Medicine* and 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 treatment with daratumumab in combination with lenalidomide (an immunomodulatory drug) and dexamethasone (a corticosteroid) or treatment with lenalidomide and dexamethasone alone. In the daratumumab treatment arm, patients received 16 milligrams per kilogram (mg/kg) weekly for the 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 is administered at 25 mg orally on days 1 through 21 of each 28-day cycle, and dexamethasone is administered at 40 mg once a week for both treatment arms. Participants in both treatment arms will continue Rd 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> Approximately 16,830 new patients were expected to be diagnosed with multiple myeloma and approximately 10,480 people were expected to die from the disease in the Western Europe in 2018.<sup>2</sup> Globally, it was estimated that 160,000 people were diagnosed and 106,000 died from the disease in 2018.<sup>3</sup> While some patients with multiple myeloma have no symptoms at all,

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most patients are diagnosed due to symptoms which can include bone problems, low blood counts, calcium elevation, kidney problems or infections.<sup>4</sup>

### About DARZALEX® (daratumumab)

DARZALEX® (daratumumab) intravenous infusion is indicated for the treatment of adult patients in the United States: in combination with bortezomib, thalidomide and dexamethasone as treatment for patients newly diagnosed with multiple myeloma who are eligible for autologous stem cell transplant; in combination with lenalidomide and dexamethasone for the treatment of 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>5</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 intravenous infusion is indicated for the treatment of adult patients in Europe: in combination with lenalidomide and dexamethasone for the treatment of 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 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<sup>6</sup>. 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 intravenous infusion is approved for the treatment of adult patients: in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone for the treatment of relapsed or refractory multiple myeloma; 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. 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>5,6,7,8,9,10</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 refractory and frontline multiple myeloma settings. Additional studies are ongoing or planned to assess the potential of daratumumab in other malignant and pre-malignant diseases in which CD38 is expressed, such as amyloidosis, NKT-cell lymphoma and B-cell and T-cell ALL. Daratumumab has received two Breakthrough Therapy Designations from the U.S. FDA for certain indications of multiple myeloma, including as a monotherapy for heavily pretreated multiple myeloma and in combination with certain other therapies for second-line treatment of multiple myeloma.

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### 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, the HexElect® platform, which combines two co-dependently acting HexaBody molecules to introduce selectivity while maximizing therapeutic potency and the DuoHexaBody® platform, which enhances the potential potency of bispecific antibodies through hexamerization. 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. Genmab is headquartered in Copenhagen, Denmark with core sites in Utrecht, the Netherlands and Princeton, New Jersey, U.S.

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Genmab A/S and/or its subsidiaries own the following trademarks: Genmab®; the Y-shaped Genmab logo®; Genmab in combination with the Y-shaped Genmab logo®; HuMax®; DuoBody®; DuoBody in combination with the DuoBody logo®; HexaBody®; HexaBody in combination with the HexaBody logo®; DuoHexaBody®; HexElect®; and UniBody®. Arzerra® is a trademark of Novartis AG or its affiliates. DARZALEX® 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> Globocan 2018. Western Europe Fact Sheet. Available at <http://gco.iarc.fr/today/data/factsheets/populations/926-western-europe-fact-sheets.pdf>. Accessed March 2018

<sup>3</sup> Globocan 2018. World Fact Sheet. Available at <http://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf>. Accessed December 2018.

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<sup>4</sup> American Cancer Society. "How is Multiple Myeloma Diagnosed?"

<http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-diagnosis>. Accessed June 2016

<sup>5</sup> DARZALEX Prescribing information, September 2019. Available at:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/761036s024lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761036s024lbl.pdf) Last accessed September 2019

<sup>6</sup> DARZALEX Summary of Product Characteristics, available at <https://www.ema.europa.eu/en/medicines/human/EPAR/darzalex> Last accessed October 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.