



## CHMP Issues Positive Opinion Recommending DARZALEX® (Daratumumab) in Combination with Lenalidomide and Dexamethasone in Frontline Multiple Myeloma

October 18, 2019

### Company Announcement

- CHMP issued a positive opinion for DARZALEX® in combination with lenalidomide and dexamethasone as treatment for newly diagnosed adult patients with multiple myeloma who are ineligible for autologous stem cell transplant
- Final decision from European Commission expected in the coming months
- Opinion based on data from Phase III MAIA study

Copenhagen, Denmark; October 18, 2019 – Genmab A/S (Nasdaq: GMB) announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion recommending broadening the existing marketing authorization for DARZALEX® (daratumumab) in the European Union. The recommendation is for the use of DARZALEX in combination with lenalidomide and dexamethasone (Rd) as treatment for newly diagnosed adult patients with multiple myeloma who are ineligible for autologous stem cell transplant (ASCT). The Type II variation application, based on the Phase III MAIA (MMY3008) study, was submitted to the EMA by Janssen Pharmaceutica NV in March 2019. In August 2012, Genmab granted Janssen Biotech, Inc. an exclusive worldwide license to develop, manufacture and commercialize daratumumab.

"We are encouraged that the CHMP are recommending a broadening of the current DARZALEX marketing authorization in the European Union to include DARZALEX in combination with lenalidomide and dexamethasone as a possible treatment for patients newly diagnosed with multiple myeloma. This would give patients another treatment option, in addition to the already approved combination of daratumumab plus bortezomib, melphalan and prednisone in this same setting," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

### 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 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, 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 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<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 is approved in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adults with relapsed or refractory multiple myeloma and 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.

#### **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 function enhanced antibodies, the HexElect<sup>®</sup> platform, which combines two co-dependently acting HexaBody molecules to introduce selectivity while maximizing therapeutic potency and the DuoHexaBody<sup>®</sup> 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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*This Company Announcement contains forward looking statements. The words "believe", "expect", "anticipate", "intend" and "plan" and similar expressions identify forward looking statements. Actual results or performance may differ materially from any future results or performance expressed or implied by such statements. The important factors that could cause our actual results or performance to differ materially include, among others, risks associated with pre-clinical and clinical development of products, uncertainties related to the outcome and conduct of clinical trials including unforeseen safety issues, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products or technologies obsolete, and other factors. For a further discussion of these risks, please refer to the risk management sections in Genmab's most recent financial reports, which are available on [www.genmab.com](http://www.genmab.com) and the risk factors included in Genmab's final prospectus for our U.S. public offering and listing and other filings with the U.S. Securities and Exchange Commission (SEC), which are available at [www.sec.gov](http://www.sec.gov). Genmab does not undertake any obligation to update or revise forward looking statements in this Company Announcement nor to confirm such statements to reflect subsequent events or circumstances after the date made or in relation to actual results, unless required by law.*

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> 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.

<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/2019/761036s024bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761036s024bl.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> Krejčík 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.

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