

## U.S. FDA Grants Priority Review for Daratumumab in Front Line Multiple Myeloma

### Company Announcement

- U.S. FDA grants Priority Review to daratumumab in combination with bortezomib, melphalan and prednisone for the treatment of patients with newly diagnosed multiple myeloma ineligible for autologous stem cell transplant
- May 21, 2018 PDUFA date

Copenhagen, Denmark; January 19, 2018 – Genmab A/S (Nasdaq Copenhagen: GEN) announced today that the U.S. Food and Drug Administration (FDA) has granted Priority Review to the supplemental Biologics License Application (sBLA) for the use of daratumumab (DARZALEX®) 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 (ASCT). The sBLA was submitted by Genmab's licensing partner, Janssen Biotech, Inc., in November 2017. Priority Review is an FDA designation for drugs that treat a serious condition and may provide a significant improvement in safety or efficacy. The FDA has assigned a Prescription Drug User Fee Act (PDUFA) target date of May 21, 2018 to take a decision on daratumumab in this indication. In August 2012, Genmab granted Janssen Biotech, Inc. an exclusive worldwide license to develop, manufacture and commercialize daratumumab.

"The granting of priority review to the submission of daratumumab in front line multiple myeloma is an important step forward towards potentially bringing this product to an even larger number of patients in need," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

The sBLA submission was based on data from the Phase III ALCYONE study of daratumumab in combination with bortezomib, melphalan and prednisone in front line multiple myeloma. This data was presented as a Late-Breaking Abstract at the 2017 American Society of Hematology (ASH) Annual Meeting and published in *The New England Journal of Medicine* in December, 2017.

#### About the ALCYONE study

This Phase III study (NCT02195479) is a randomized, open-label, multicenter study and includes 706 newly diagnosed patients with multiple myeloma who are ineligible for autologous stem cell transplantation (ASCT). Patients were randomized to receive 9 cycles of either VMP [bortezomib (a proteasome inhibitor), melphalan (an alkylating chemotherapeutic agent) and prednisone (a corticosteroid)] combined with daratumumab, or VMP alone. In the daratumumab treatment arm, patients received 16 mg/kg of daratumumab once weekly for six weeks (cycle 1; 1 cycle = 42 days), followed by once every three weeks (cycles 2-9). Following the 9 cycles, patients in the daratumumab treatment arm continued to receive 16 mg/kg of daratumumab once every four weeks until disease progression. The primary endpoint 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 30,330 new patients were expected to be diagnosed with multiple myeloma and approximately 12,650 people were expected to die from the disease in the U.S. in 2016.<sup>3</sup> Globally, it was estimated that 124,225 people would be diagnosed and 87,084 would die from the disease in 2015.<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> Patients who relapse after treatment with standard therapies, including proteasome inhibitors or immunomodulatory agents, have poor prognoses and few treatment options.<sup>6</sup>

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

DARZALEX<sup>®</sup> (daratumumab) injection for intravenous infusion is indicated in the United States 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 (FDA) approval to treat multiple myeloma. DARZALEX is indicated in Europe 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. In Japan, DARZALEX is approved in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for treatment of adults with relapsed or refractory multiple myeloma. DARZALEX is the first human CD38 monoclonal antibody to reach the market. 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>7,8,9,10,11</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 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 on which CD38 is expressed, such as smoldering myeloma, NKT-cell lymphoma, myelodysplastic syndromes and solid tumors. 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 solid tumors. 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, and the HexaBody<sup>®</sup> platform which creates effector function enhanced antibodies. 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 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>; the DuoBody logo<sup>®</sup>; the HexaBody logo<sup>™</sup>; HuMax<sup>®</sup>; HuMax-CD20<sup>®</sup>; DuoBody<sup>®</sup>; HexaBody<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 Biotech, Inc.

<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> American Cancer Society. "What are the key statistics about multiple myeloma?" <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-key-statistics>. Accessed June 2016.

<sup>4</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 June 2016.

<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> Kumar, SK et al. Risk of progression and survival in multiple myeloma relapsing after last therapy with IMiDs and bortezomib: a multicenter international myeloma working group study. *Leukemia*. 2012; 26:149-57.

<sup>7</sup> DARZALEX Prescribing information, June 2017. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2017/761036s005lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761036s005lbl.pdf) Last accessed June 2017

<sup>8</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>9</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>10</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>11</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.