



Genmab Announces Approval of DARZALEX® (daratumumab) in Frontline Multiple Myeloma in Japan

August 22, 2019

Company Announcement

- **DARZALEX® approved in combination with bortezomib, melphalan and prednisone for the treatment of patients with newly diagnosed multiple myeloma ineligible for autologous stem cell transplant in Japan**
- **Genmab to receive USD 7 million milestone payment**
- **Approval based on data from Phase III ALCYONE study**

Copenhagen, Denmark; August 22, 2019 – Genmab A/S (Nasdaq: GMB) announced today that the Ministry of Health, Labor and Welfare (MHLW) in Japan has approved the use of DARZALEX (daratumumab) 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). DARZALEX is being developed under an August 2012 agreement in which Genmab granted Janssen Biotech, Inc. (Janssen) an exclusive worldwide license to develop, manufacture and commercialize the product. Genmab will receive a USD 7 million milestone payment from Janssen in connection with the approval and first commercial sale of DARZALEX under the newly expanded label. The approval and related milestone do not impact the financial guidance issued by Genmab on August 14, 2019.

“Multiple myeloma remains one of the most common forms of blood cancer in Japan and as such, we are encouraged that patients in Japan newly diagnosed with this disease now have the option to receive a DARZALEX containing regimen,” said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

The approval is based on data from the Phase III ALCYONE study that showed a reduction of the risk of disease progression or death by 50 percent in newly diagnosed ASCT ineligible multiple myeloma patients when daratumumab is combined with bortezomib, melphalan and prednisone. 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 that included 706 newly diagnosed patients with multiple myeloma who are ineligible for 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), once every three weeks from cycles 2 to 9, once every four weeks from cycle 9 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.¹ Approximately 6,313 new patients were expected to be diagnosed with multiple myeloma and approximately 4,338 people were expected to die from the disease in Japan in 2018.² Globally, it was estimated that 160,000 people were diagnosed and 106,000 died from the disease in 2018.³ 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.⁴

About DARZALEX® (daratumumab)

DARZALEX® (daratumumab) intravenous infusion is indicated for the treatment of adult patients in the United States: 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.⁵ 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 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.

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).^{5,6,7,8,9}

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[®] (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.

Contact:

Marisol Peron, Corporate Vice President, Communications & Investor Relations
T: +1 609 524 0065; E: mmp@genmab.com

For Investor Relations:

Andrew Carlsen, Senior Director, Investor Relations
T: +45 3377 9558; E: acn@genmab.com

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

² Globocan 2018. Japan Fact sheet. Available at <http://gco.iarc.fr/today/data/factsheets/populations/392-japan-fact-sheets.pdf> Accessed March 2019

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

⁴ American Cancer Society. "How is Multiple Myeloma Diagnosed?" <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-diagnosis>. Accessed June 2016.

⁵ DARZALEX Prescribing information, July 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761036s019lbl.pdf Last accessed July 2019

⁶ 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.

⁷ 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.

⁸ 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.

⁹ 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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Genmab A/S
Kalvebod Brygge 43
1560 Copenhagen V
Denmark

Attachment

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