



Genmab Announces Janssen Granted U.S. FDA Approval for DARZALEX® (daratumumab) in Combination with Carfilzomib and Dexamethasone in Relapsed or Refractory Multiple Myeloma

August 20, 2020

Company Announcement

- **DARZALEX® (daratumumab) approved by U.S. FDA in combination with carfilzomib and dexamethasone for the treatment of adult patients with relapsed/refractory multiple myeloma who have received one to three previous lines of therapy**
- **Approval based on the Phase 3 CANDOR study**
- **Approval marks eighth U.S. FDA approval for DARZALEX**

Copenhagen, Denmark; August 20, 2020 – Genmab A/S (Nasdaq: GMAB) announced today that the U.S. Food and Drug Administration (U.S. FDA) has approved the use of DARZALEX® (daratumumab) in combination with carfilzomib and dexamethasone (DKd) for the treatment of adult patients with relapsed/refractory multiple myeloma who have received one to three previous lines of therapy. A supplemental Biologics License Application (sBLA) for this indication was submitted by Genmab's licensing partner, Janssen Biotech, Inc. (Janssen), in February 2020. In August 2012, Genmab granted Janssen an exclusive worldwide license to develop, manufacture and commercialize daratumumab.

"We are extremely pleased that multiple myeloma patients in the U.S. will now have yet another treatment option as this is the eighth overall U.S. FDA approval for DARZALEX and the fifth in the relapsed/refractory setting. In addition, DARZALEX is now the first CD38 antibody approved for use in combination with carfilzomib," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

The combination has been approved in two carfilzomib dosing regimens, 70 mg/m² once weekly and 56 mg/m² twice weekly, based on positive results from the Phase 3 CANDOR and Phase 1b EQUULEUS studies. CANDOR was an Amgen-sponsored study, co-funded by Janssen Research & Development, LLC. EQUULEUS was sponsored by Janssen Research & Development, LLC.

About the CANDOR study

The Phase 3 trial (NCT03158688) was a randomized, open-label study that included 466 patients with multiple myeloma who had relapsed after 1 to 3 prior therapies. Patients were randomized to receive either DKd or carfilzomib and dexamethasone (Kd) alone. In the daratumumab treatment arm, patients received 8 milligrams per kilogram (mg/kg) on days 1 and 2 of cycle 1, then 16 mg/kg once weekly for the remaining doses of the first 2 cycles, then every 2 weeks for 4 cycles (cycles 3 to 6), and then every 4 weeks for the remaining cycles or until disease progression. In both treatment arms carfilzomib was dosed twice weekly (20 mg/m² on cycle 1 days 1 and 2 and 56 mg/m² beginning on cycle 1 day 8 and thereafter) and dexamethasone was given weekly (40 mg orally or via IV infusion). The primary endpoint of the study was progression free survival (PFS).

About the EQUULEUS (MMY1001) Study

The Phase 1b EQUULEUS (NCT01998971) study was an open label, multi-cohort trial that evaluated the safety, tolerability, and dose regimen of daratumumab when administered in combination with various treatment regimens for the treatment of multiple myeloma. Among the regimens evaluated, the combination of DKd compared to Kd alone was studied in 85 patients with relapsed/refractory multiple myeloma who had received one to three prior lines of therapy using a once-weekly dosing regimen. DKd was evaluated at a starting dose of 20 mg/m², which was increased to 70 mg/m² on Cycle 1, Day 8 and onward.

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 Multiple myeloma is the third most common blood cancer in the U.S., after leukemia and lymphoma.² 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 2018.³ Globally, it was estimated that 160,000 people were diagnosed and 106,000 died from the disease in 2018.⁴ 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.⁵

About DARZALEX® (daratumumab)

DARZALEX® (daratumumab) has become a backbone therapy in the treatment of multiple myeloma. DARZALEX intravenous infusion is indicated for the treatment of adult patients in the United States: in combination with carfilzomib and dexamethasone for the treatment of patients with relapsed/refractory multiple myeloma who have received one to three previous lines of therapy; 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.⁶ 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 for the treatment of adult patients in Europe via intravenous infusion or subcutaneous administration: 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 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 therapy⁷. Daratumumab is the first subcutaneous CD38 antibody approved in Europe for the treatment of multiple myeloma. 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 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 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.

DARZALEX FASPRO™ (daratumumab and hyaluronidase-fihj), a subcutaneous formulation of daratumumab, is approved in the United States for the treatment of adult patients with multiple myeloma: in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for ASCT; in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for ASCT and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy; in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy; and as monotherapy, in patients 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.⁸ DARZALEX FASPRO is the first subcutaneous CD38 antibody approved in the U.S. for the treatment of multiple myeloma.

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).^{6,9,10,11,12}

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 and T-cell acute lymphocytic leukemia (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 is the creator of the following approved antibodies: DARZALEX® (daratumumab, under agreement with Janssen Biotech, Inc.) for the treatment of certain multiple myeloma indications in territories including the U.S., Europe and Japan, Kesimpta® (subcutaneous ofatumumab, under agreement with Novartis AG), for the treatment of adults with relapsing forms of multiple sclerosis in the U.S. and TEPEZZA® (teprotumumab, under agreement with Roche granting sublicense to Horizon Therapeutics plc) for the treatment of thyroid eye disease in the U.S. A subcutaneous formulation of daratumumab, known as DARZALEX FASPRO™ (daratumumab and hyaluronidase-fihj) in the U.S., has been approved in the U.S. and Europe for the treatment of adult patients with certain multiple myeloma indications. The first approved Genmab created therapy, Arzerra® (ofatumumab, under agreement with Novartis AG), approved for the treatment of certain chronic lymphocytic leukemia indications, is available in Japan and is also available in other territories via compassionate use or oncology access programs. Daratumumab is in clinical development by Janssen for the treatment of additional multiple myeloma indications, other blood cancers and amyloidosis. 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 sites in Utrecht, the Netherlands, Princeton, New Jersey, U.S. and Tokyo, Japan.

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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 and the risk factors included in Genmab's most recent Annual Report on Form 20-F and other filings with the U.S. Securities and Exchange Commission (SEC), which are available at 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.

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- ⁴ 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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- ¹¹ 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.
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