Genmab Announces Submission of Biologics License Application to U.S. FDA for Subcutaneous Formulation of Daratumumab

July 12, 2019

Company Announcement

- **BLA submitted to U.S. FDA for subcutaneous formulation of daratumumab**
- **Submission based on data from Phase III COLUMBA and Phase II PLEIADES studies**

Copenhagen, Denmark; July 12, 2019 – Genmab A/S (Nasdaq Copenhagen: GEN) announced today that its licensing partner, Janssen Biotech, Inc., has submitted a Biologics License Application (BLA) to the U.S. Food and Drug Administration (U.S. FDA) for the use of the subcutaneous (SubQ) formulation of daratumumab in multiple myeloma indications where the intravenous formulation of daratumumab is currently approved. In August 2012, Genmab granted Janssen an exclusive worldwide license to develop, manufacture and commercialize daratumumab.

"Should this submission lead to an approval, it would provide patients with a treatment option that combines efficacy comparable with intravenous DARZALEX® with a subcutaneous delivery that reduces treatment time from hours to just minutes. Not only would this be more convenient for patients but, as we saw with the COLUMBA data recently presented at the 2019 ASCO Annual Meeting and 24th EHA Annual Congress, infusion-related reactions are both mild and significantly reduced with this formulation of daratumumab," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab. "Subcutaneous daratumumab may also provide an attractive option for health care providers, especially in the community setting, where reducing the administration time can be very important."

The submission is based on data from two ongoing studies: the Phase III non-inferiority COLUMBA study, which is comparing the subcutaneous formulation of daratumumab to the intravenous formulation in patients with relapsed or refractory multiple myeloma and preliminary non-public data from the Phase II PLEIADES study, which is evaluating daratumumab in combination with certain standard multiple myeloma regimens. The topline results from the COLUMBA data were announced in February 2019 and subsequently presented in oral sessions at the 2019 American Society of Clinical Oncology Annual Meeting and the 24th European Hematology Association Annual Congress.

About the COLUMBA (MMY3012) study
The Phase III trial (NCT03277105) is a randomized, open-label, parallel assignment study that includes 522 adults diagnosed with relapsed and refractory multiple myeloma. Patients were randomized to receive either: SubQ daratumumab, as 1800 mg daratumumab with rHuPH20 2000 U/mL once weekly in Cycle 1 and 2, every two weeks in Cycle 3 to 6, every 4 weeks in Cycle 7 and thereafter until disease progression, unacceptable toxicity or the end of study; or 16 mg/kg IV daratumumab once weekly in Cycle 1 and 2, every two weeks in Cycle 3 to 6, every 4 weeks in Cycle 7 and thereafter until disease progression, unacceptable toxicity or the end of study. The co-primary endpoints of the study are overall response rate and Maximum trough concentration of daratumumab (C_{trough}; defined as the serum pre-dose concentration of daratumumab on Cycle 3 Day 1).

About the PLEIADES (MMY2040) study
The Phase II trial (NCT03412565) is a non-randomized, open-label, parallel assignment study that includes 240 adults either newly diagnosed or with relapsed or refractory multiple myeloma. Patients with newly diagnosed multiple myeloma are being treated with 1,800 mg subcutaneous daratumumab in combination with either bortezomib, lenalidomide and dexamethasone (D-VRd) or bortezomib, melphalan and prednisone (D-VMP). Patients with relapsed or refractory multiple myeloma are being treated with 1,800 mg subcutaneous daratumumab plus lenalidomide and dexamethasone (D-Rd). An additional cohort of patients with relapsed and refractory multiple myeloma treated with daratumumab plus carfilzomib and dexamethasone (D-Kd) was subsequently added to the study. The primary endpoint for the D-VMP, D-Kd and D-Rd cohorts is overall response rate. The primary endpoint for the D-VRd cohort is very good partial response or better rate.

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.[1] 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. DARZALEX is the first human CD38 monoclonal antibody to reach the market in the United Stated, Europe and Japan.

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).[1,2,3,4,5]

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 includes a number of proprietary next generation antibody. Genmab has alliances with other leading pharmaceutical and biotechnology companies.

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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 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. 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.

[1] DARZALEX Prescribing information, June 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761036s020lbl.pdf Last accessed June 2019
[2] 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.
[3] 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.
[4]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.
[5]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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Attachment

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