

## Data from Phase III POLLUX Study of Daratumumab Published in The New England Journal of Medicine

### Media Release

- The New England Journal of Medicine published data from the Phase III POLLUX study of daratumumab in relapsed or refractory multiple myeloma
- Study data initially presented at the 21<sup>st</sup> Congress of EHA

**Copenhagen, Denmark; October 6, 2016 – Genmab A/S (Nasdaq Copenhagen: GEN) announced today The New England Journal of Medicine has published data from the Phase III POLLUX (MMY3003) study of daratumumab.** The POLLUX data were presented at the 21<sup>st</sup> Congress of the European Hematology Association (EHA) in June. Daratumumab was granted a Breakthrough Therapy Designation (BTD) from the U.S. Food and Drug Administration (FDA) based on these data in July 2016.

The Phase III POLLUX study enrolled 569 patients who had relapsed or refractory multiple myeloma. Patients were randomized to receive either daratumumab combined with lenalidomide (an immunomodulatory drug) and dexamethasone (a corticosteroid), or lenalidomide and dexamethasone alone. The study met the primary endpoint of improving progression-free survival (PFS) (Hazard Ratio (HR) = 0.37; 95% CI 0.27-0.52; p<0.001) for patients treated with daratumumab versus patients who did not receive daratumumab. Patients who received treatment with daratumumab in combination with lenalidomide and dexamethasone had a 63% reduction in risk of their disease progressing, compared to those who did not receive daratumumab. The median PFS for patients treated with daratumumab in combination with lenalidomide and dexamethasone has not been reached, compared to an estimated median PFS of 18.4 months for patients who received lenalidomide and dexamethasone alone. The overall response rate was 93% in the group of patients treated with daratumumab versus 76% in the group that did not receive daratumumab. The rates of very good partial response or better (76% vs 44%) and complete response or better (43% vs 19%) were also higher for the group treated with daratumumab. Of patients treated with daratumumab, 22% were minimal residual disease negative, versus 5% in those who did not receive daratumumab; negative minimal residual disease translated into improved outcomes. The most common grade 3 or 4 adverse events in patients treated with daratumumab in combination with lenalidomide and dexamethasone versus those who received only lenalidomide and dexamethasone were neutropenia (51.9% vs 37.0%), thrombocytopenia (12.7% vs 13.5%), and anemia (12.4% vs 19.6%). Daratumumab-associated infusion-related reactions occurred in 48% of patients, were mostly grade 1/2, and occurred predominantly during the first infusion. Overall, the safety profile was consistent with known toxicities of daratumumab monotherapy and combination therapy of lenalidomide and dexamethasone.

Data from another Phase III study (CASTOR) of daratumumab combined with subcutaneous bortezomib (a type of chemotherapy, called a proteasome inhibitor) and dexamethasone (a corticosteroid) compared with bortezomib and dexamethasone alone in patients with relapsed or refractory multiple myeloma was also recently published in the New England Journal of Medicine.<sup>1</sup>

“Following the publication of the Phase III CASTOR data, we are pleased that the positive data from the Phase III POLLUX study has now also been published in the New England Journal of Medicine,” said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab. “The data from this study formed the basis, along with data from the CASTOR study, of two regulatory submissions in August; the supplemental Biologics License Application submitted to the U.S. Food and Drug Administration and the submission of the variation to the Marketing Authorization to the European Medicines Agency.”

### 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>2</sup> Multiple myeloma is the third most common blood cancer in the U.S., after leukemia and lymphoma.<sup>3</sup> Approximately 30,330 new patients are expected to be diagnosed

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with multiple myeloma and approximately 12,650 people are expected to die from the disease in the U.S. in 2016.<sup>4</sup> Globally, it was estimated that 124,225 people would be diagnosed and 87,084 would die from the disease in 2015.<sup>5</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>6</sup> Patients who relapse after treatment with standard therapies, including proteasome inhibitors or immunomodulatory agents, have poor prognoses and few treatment options.<sup>7</sup>

### About DARZALEX® (daratumumab)

DARZALEX® (daratumumab) injection for intravenous infusion is indicated in the United States for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent, or who are double-refractory to a PI and an immunomodulatory agent.<sup>8</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 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. 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. It is believed to induce rapid tumor cell death through programmed cell death, or apoptosis,<sup>8,9</sup> and multiple immune-mediated mechanisms, including complement-dependent cytotoxicity,<sup>8,9</sup> antibody-dependent cellular phagocytosis<sup>10,11</sup> and antibody-dependent cellular cytotoxicity.<sup>8,9</sup> In addition, daratumumab therapy results in a reduction of immune-suppressive myeloid derived suppressor cells (MDSCs) and subsets of regulatory T cells (Tregs) and B cells (Bregs), all of which express CD38. These reductions in MDSCs, Tregs and Bregs were accompanied by increases in CD4+ and CD8+ T cell numbers in both the peripheral blood and bone marrow.<sup>8,12</sup>

Daratumumab is being developed by Janssen Biotech, Inc. under an exclusive worldwide license to develop, manufacture and commercialize daratumumab from Genmab. Five Phase III clinical studies with daratumumab in relapsed and frontline settings are currently ongoing, and additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant diseases on which CD38 is expressed, such as smoldering myeloma, non-Hodgkin's lymphoma and a solid tumor.

### 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, Arzerra® (ofatumumab) for the treatment of certain chronic lymphocytic leukemia indications and DARZALEX® (daratumumab) for the treatment of heavily pretreated or double refractory multiple myeloma. Daratumumab is in clinical development for additional multiple myeloma indications and for non-Hodgkin's lymphoma. 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, and the HexaBody® 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).

### Contact:

Rachel Curtis Gravesen, Senior Vice President, Investor Relations & Communication  
T: +45 33 44 77 20; M: +45 25 12 62 60; E: [r.gravesen@genmab.com](mailto:r.gravesen@genmab.com)

*This Media Release contains forward looking statements. The words "believe", "expect", "anticipate", "intend" and "plan" and similar*

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<sup>1</sup> Palumbo, A et al. Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2016; 375: 754–766.

<sup>2</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>3</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>4</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>5</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>6</sup> American Cancer Society. "How is Multiple Myeloma Diagnosed?"

<http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-diagnosis>. Accessed June 2016.

<sup>7</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>8</sup> DARZALEX US Prescribing Information, November 2015.

<sup>9</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>10</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>11</sup> Khagi, Y and Mark, TM. Potential role of daratumumab in the treatment of multiple myeloma. Onco Targets Ther. 2014; 7: 1095–1100.

<sup>12</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.