# Genmab Provides Update on Marketing Authorization Application for Arzerra® (ofatumumab) as Maintenance Therapy for Patients with Relapsed CLL

## Company Announcement

- **Committee for Medicinal Products for Human Use (CHMP) issues negative opinion for Arzerra for maintenance treatment of patients with relapsed CLL**

**Copenhagen, Denmark; June 23, 2016 – Genmab A/S (Nasdaq Copenhagen: GEN) announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a negative opinion for the use of Arzerra® (ofatumumab) as maintenance therapy for patients with relapsed chronic lymphocytic leukemia (CLL).** The Marketing Authorization Application (MAA) was submitted by Novartis in July 2015 under the ofatumumab collaboration between Novartis and Genmab.

"We are disappointed that we did not receive a positive recommendation for Arzerra in the maintenance CLL setting in Europe. We will continue to work with Novartis to define the best path forward for Arzerra," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

The MAA was based on positive data from an interim analysis from the Phase III PROLONG study (OMB112517), which evaluated ofatumumab maintenance therapy versus no further treatment in patients with a complete or partial response after second or third line treatment for CLL.

**Safety and Efficacy Data from the Phase III PROLONG study**
A total of 474 patients were included in the analysis. Patients who received ofatumumab maintenance treatment lived 14.2 months longer without their disease worsening than patients who received no further treatment. Median progression free survival (PFS) as assessed by the investigators was 29.4 months for the ofatumumab treatment arm, and 15.2 months for the observation arm (Hazard Ratio 0.50; $p<0.0001$).

There were no unexpected safety findings. The most common adverse reactions (≥10%) were infusion reactions, neutropenia, and upper respiratory tract infection. The two most common grade 3-4 adverse events were neutropenia (22% in ofatumumab arm vs 8% in observation arm), and pneumonia (5% in ofatumumab arm vs 3% in observation arm). During the period between the first dose and 60 days after the last dose there were two patients (1%) in the ofatumumab group and five patients (2%) in the observation group who died due to adverse events.

**About the Phase III PROLONG study**
This Phase III study was designed to randomize up to 532 patients with relapsed CLL who have responded to treatment at relapse, to either ofatumumab maintenance treatment or no further treatment (observation). Patients in the ofatumumab arm received an initial dose of 300 mg of ofatumumab, followed one week later by a second dose of 1,000 mg, then doses of 1,000 mg every 8 weeks for up to two years, while patients in the observation treatment arm received no further treatment.

The primary endpoint of the study was PFS. Secondary objectives were evaluation of clinical benefit, overall survival, safety, tolerability, the health-related quality of life of subjects treated with ofatumumab versus no further treatment, and pharmacokinetics among relapsed CLL patients receiving maintenance therapy with ofatumumab.

**About CLL**
CLL is the most commonly diagnosed adult leukemia in Western countries, and accounts for approximately 1 in 4 cases of leukemia.[1] Most CLL patients experience disease progression despite initial response to therapy and may require additional treatment.[2]

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**About Ofatumumab (Arzerra®)**
Ofatumumab is a human monoclonal antibody that is designed to target the CD20 molecule found on the surface of chronic lymphocytic leukemia (CLL) cells and normal B lymphocytes.

In the United States, Arzerra is approved for use in combination with chlorambucil for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate and for extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive CLL. In the European Union, Arzerra is approved for use in combination with chlorambucil or bendamustine for the treatment of patients with CLL who have not received prior therapy and who are not eligible for fludarabine-based therapy. In more than 50 countries worldwide, Arzerra is also indicated as monotherapy for the treatment of patients with CLL who are refractory after prior treatment with fludarabine and alemtuzumab.

Please see full Prescribing Information, including Boxed WARNING for Arzerra (ofatumumab).

Arzerra is marketed under a collaboration agreement between Genmab and Novartis. Novartis has rights to develop ofatumumab in autoimmune indications, including multiple sclerosis.

**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.

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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 in relation to actual results, unless required by law.*



**References**

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[1] GlobalData. EpiCast Report: Chronic Lymphocytic Leukemia Epidemiology Forecast to 2023. Published May 2014.
[2] Veliz M, Pinilla-Ibarz J. Treatment of relapsed or refractory chronic lymphocytic leukemia. Cancer Control. 2012; 1:37-53.