

Genmab Announces Additional Data from Phase III Study of Ofatumumab as Maintenance Therapy for Relapsed CLL

Company Announcement

- 13.4 month improvement in median progression free survival in patients receiving ofatumumab maintenance therapy for relapsed CLL
- Data to be presented in oral session at ASH Annual Meeting in December

Copenhagen, Denmark; November 6, 2014 – Genmab A/S (OMX: GEN) announced today additional data from the interim analysis of the ofatumumab (Arzerra™) Phase III study, PROLONG (OMB112517). The study evaluated ofatumumab maintenance therapy versus no further treatment (observation) in patients with a complete response (CR) or partial response (PR) after 2nd or 3rd line treatment for chronic lymphocytic leukemia (CLL). The improvement in the study's primary endpoint, progression free survival (PFS), met the prespecified statistical significance level for the interim analysis.

A total of 474 patients were included in the interim analysis. Patients who received ofatumumab maintenance treatment lived 13.4 months longer without their disease worsening (median PFS) than patients who received no further treatment. Median PFS was 28.6 months for the ofatumumab treatment arm and 15.2 months for the observation arm (Hazard Ratio 0.48; $p < 0.0001$).

The amount of time until patients started their next therapy was significantly longer in the ofatumumab treatment arm than in the observation arm (median 38.0 months vs 27.4 months, Hazard Ratio 0.63; $p = 0.0076$).

There were no unexpected safety findings. Adverse events occurred in 87% of patients in the ofatumumab treatment arm versus 75% in the observation treatment arm. In the ofatumumab treatment arm, 25% of patients experienced grade 3-4 adverse events compared to 17% in the observation arm. Grade 3-4 infections were 18% in the ofatumumab arm and 13% in the observation arm. The two most common grade 3-4 adverse events were neutropenia (22% in ofatumumab arm vs 9% in observation arm), and pneumonia (7% in ofatumumab arm vs 4% in observation arm). The death rate was similar in both arms (14%).

"The interim results of this study show that ofatumumab maintenance therapy significantly extended the amount of time the patients in the study lived without their CLL symptoms getting worse," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

These data will be presented in an oral session at the 56th Annual Meeting of the American Society of Hematology (ASH) in San Francisco, California on December 6 from 12 Noon to 1:30PM PST.

About PROLONG

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). The study is no longer recruiting patients. 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 is PFS. Secondary objectives will evaluate 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.

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About CLL

CLL, the most commonly diagnosed adult leukaemia in western countries, accounts for approximately one-third of all cases of leukemia.^{1,2,3} In the USA, it is estimated that more than 105,000 people currently live with or have been previously treated for CLL and an estimated 15,680 new cases of CLL were diagnosed in the past year.^{3,4} The average age of diagnosis is 72 years, and approximately 90 percent of patients with CLL are estimated to be over the age of 55 years.^{3,5}

About ofatumumab (Arzerra)

Ofatumumab—a monoclonal antibody that is designed to target the CD20 molecule found on the surface of CLL cells and normal B lymphocytes—is not approved or licensed anywhere in the world as maintenance treatment for relapsed CLL.

In the USA, ofatumumab 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. In the EU, ofatumumab 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, ofatumumab is indicated as monotherapy for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.

Ofatumumab is being developed under a co-development and collaboration agreement between Genmab and GSK.

Important Safety Information for ofatumumab (Arzerra)

The overall safety profile of ofatumumab in CLL (previously untreated and relapsed or refractory) is based on data from more than 800 patients treated alone or in combination with other therapies in clinical trials.

The most common undesirable effects for ofatumumab include adverse events associated with infusion reactions, cytopenias (neutropenia, anemia, febrile neutropenia, thrombocytopenia, leukopenia), and infections (lower respiratory tract infection, including pneumonia, upper respiratory tract infection, sepsis, including neutropenic sepsis and septic shock, herpes virus infection, urinary tract infection).

Contraindications:

Hypersensitivity to ofatumumab or to any of the excipients.

Special warnings and precautions for use of ofatumumab are summarized as follows:

Infusion reactions

Ofatumumab has been associated with infusion reactions. These reactions may result in temporary interruption or withdrawal of treatment or death. Pre-medications attenuate infusion reactions but these may still occur, predominantly during the first infusion. Infusion reactions may include, but are not limited to, anaphylactic reactions, bronchospasm, cardiac events (eg myocardial ischemia / infarction, bradycardia), chills/rigors, cough, cytokine release syndrome, diarrhea, dyspnoea, fatigue, flushing, hypertension, hypotension, nausea, pain, pulmonary edema, pruritus, pyrexia, rash, and urticaria. Even with pre-medication, severe reactions, including cytokine release syndrome, have been reported following ofatumumab use. In cases of severe infusion reaction, the infusion of ofatumumab must be interrupted immediately and symptomatic treatment instituted (see Dosage and Administration for changes to infusion rates following infusion reactions).

Infusion reactions occur more frequently on the first day of infusion and tend to decrease with subsequent infusions. Patients with a history of decreased pulmonary function may be at a greater risk for pulmonary

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complications from severe reactions and should be monitored closely during infusion of ofatumumab.

Tumor lysis syndrome

In patients with CLL, tumor lysis syndrome (TLS) may occur with use of ofatumumab. Risk factors for TLS include a high tumor burden, high concentrations of circulating cells ($\geq 25,000/\text{mm}^3$), hypovolemia, renal insufficiency, elevated pre-treatment uric acid levels and elevated lactate dehydrogenase levels. Management of TLS includes correction of electrolyte abnormalities, monitoring of renal function, maintenance of fluid balance and supportive care.

Progressive multifocal leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) and death has been reported in CLL patients receiving cytotoxic pharmacotherapy, including ofatumumab. If a diagnosis of PML is suspected, ofatumumab should be discontinued and referral to a neurologist should be considered.

Immunizations

The safety of, and ability to generate a primary or anamnestic response to, immunization with live attenuated or inactivated vaccines during treatment with ofatumumab has not been studied.

Hepatitis B

Hepatitis B virus (HBV) infection and reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, has occurred in patients treated with drugs classified as CD20-directed cytolytic antibodies, including ofatumumab. All patients should be screened for HBV infection before initiation of ofatumumab treatment, patients previously exposed to HBV should be followed closely in consultation with an expert in this disease. Patients with evidence of prior HBV infection should be monitored for clinical and laboratory signs of hepatitis or HBV reactivation.

Cardiovascular

Patients with a history of cardiac disease should be monitored closely. Ofatumumab should be discontinued in patients who experience serious or life-threatening cardiac arrhythmias. The effect of multiple doses of ofatumumab on the QTc interval was evaluated in a pooled analysis of three open-label studies in patients with CLL (N=85). Increases above 5 msec were observed in the median/mean QT/QTc intervals in the pooled analysis. No large changes in the mean QTc interval (ie, >20 milliseconds) were detected.

Bowel obstruction

Bowel obstruction has been reported in patients receiving anti-CD20 monoclonal antibody therapy, including ofatumumab. Patients who present with abdominal pain, especially early in the course of ofatumumab therapy, should be evaluated and appropriate treatment instituted.

For the full US Prescribing Information, including Boxed Warning, visit <https://www.gsksource.com/gskprm/htdocs/documents/ARZERRA.PDF>. For the full EU Summary of Product Characteristics (SPC) visit <http://health.gsk.com/>.

About Genmab A/S

Genmab is a publicly traded, international biotechnology company specializing in the creation and development of differentiated human antibody therapeutics for the treatment of cancer. Founded in 1999, the company currently has one marketed antibody, Arzerra™ (ofatumumab) for the treatment of certain chronic lymphocytic leukemia indications, a clinical pipeline with both late and early stage programs, and an innovative pre-clinical 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. Genmab's deep antibody

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expertise is expected to provide a stream of future product candidates. Partnering of selected innovative product candidates and technologies is a key focus of Genmab's strategy and the company has alliances with top tier pharmaceutical and biotechnology companies. For more information visit www.genmab.com.

Contact:

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

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¹ Wadhwa P, Morrison VA. Infectious complications of chronic lymphocytic leukemia. *Seminars in Oncology*. 2006;33:240-249. <http://www.cllsupport.org.uk/infections.pdf>. Accessed February 12, 2014.

² Leukemia & Lymphoma Society. Chronic Lymphocytic Leukemia. <http://www.lls.org/#/diseaseinformation/leukemia/chroniclymphocyticleukemia/>. Accessed January 3, 2014.

³ American Cancer Society. What are the key statistics for chronic lymphocytic leukemia? <http://www.cancer.org/cancer/leukemia-chroniclymphocyticcll/detailedguide/leukemia-chronic-lymphocytic-key-statistics>. Accessed January 3, 2014.

⁴ Leukemia & Lymphoma Society. The CLL Guide. <http://www.lls.org/content/nationalcontent/resourcecenter/freeeducationmaterials/leukemia/pdf/cllguide.pdf>. Accessed January 3, 2014.

⁵ Eichhorst B, Hallek M, Dreyling M. Chronic lymphocytic leukemia: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol*. 2011;22 Suppl 2, 50-54. http://annonc.oxfordjournals.org/content/22/suppl_2/vi50.full. Accessed January 3, 2014.