Genmab Announces U.S. FDA Approval of Arzerra® (ofatumumab) as Extended Treatment for Recurrent or Progressive CLL

Company Announcement

- **Arzerra now approved by U.S. FDA for use for extended treatment of patients with recurrent or progressive CLL**
- **Approval based on data from interim analysis of Phase III PROLONG study**
- **Arzerra previously approved to treat previously untreated and refractory CLL indications in the US**

Copenhagen, Denmark; January 19, 2016 – Genmab A/S (Nasdaq Copenhagen: GEN) announced today that the U.S. Food and Drug Administration (FDA) has approved a supplemental Biologics License Application (sBLA) for the use of Arzerra® (ofatumumab) for extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive chronic lymphocytic leukemia (CLL). The application was submitted by Novartis under the ofatumumab collaboration between the two companies.

This FDA approval is based on data from an interim analysis from a Phase III study, PROLONG (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.

"The approval of Arzerra in the U.S. as extended treatment provides patients with relapsed CLL with a new treatment option that can help delay disease progression," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

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; $p<0.0001$).[1]

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 last dose there were two patients (1%) in the ofatumumab group who died due to adverse events and five patients (2%) in the observation group.[1]

About CLL
CLL, the most commonly diagnosed adult leukemia in Western countries, accounts for approximately 1 in 4 cases of leukemia.[2,3] Most CLL patients experience disease progression despite initial response to therapy and may require additional treatment.[4]

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). 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 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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Important Safety Information
The following Important Safety Information is based on the Highlights section of the Prescribing Information for Arzerra. Please consult the full prescribing information for all the labeled safety information for Arzerra.

WARNING: HEPATITIS B VIRUS REACTIVATION AND PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY[1]

- **Hepatitis B Virus (HBV) reactivation can occur in patients receiving CD20-directed cytolytic antibodies, including Arzerra®, in some cases resulting in fulminant hepatitis, hepatic failure, and death.**
- **Progressive Multifocal Leukoencephalopathy (PML) resulting in death can occur in patients receiving CD20-directed cytolytic antibodies, including Arzerra.**

Infusion Reactions[1]
Arzerra can cause serious, including fatal, infusion reactions manifesting as bronchospasm, dyspnea, laryngeal edema, pulmonary edema, flushing, hypertension, hypotension, syncope, cardiac events (e.g., myocardial ischemia/infarction, acute coronary syndrome, arrhythmia, bradycardia), back pain, abdominal pain, pyrexia, rash, urticaria, angioedema, cytokine release syndrome, and anaphylactoid/anaphylactic reactions. Infusion reactions occur more frequently with the first two infusions. These reactions may result in temporary interruption or withdrawal of treatment.

Hepatitis B Virus Reactivation[1]
Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, has occurred in patients treated with Arzerra. Cases have been reported in patients who are hepatitis B surface antigen (HBsAg) positive and also in patients who are HBsAg negative but are hepatitis B core antibody (anti-HBc) positive. Reactivation also has occurred in patients who appear to have resolved hepatitis B infection (i.e., HBsAg negative, anti-HBc positive, and hepatitis B surface antibody [anti-HBs] positive).

HBV reactivation is defined as an abrupt increase in HBV replication manifesting as a rapid increase in serum HBV DNA level or detection of HBsAg in a person who was previously HBsAg negative and anti-HBc positive. Reactivation of HBV replication is often followed by hepatitis, i.e., increase in transaminase levels and, in severe cases, increase in bilirubin levels, liver failure, and death.

Hepatitis B Virus Infection[1]
Fatal infection due to hepatitis B in patients who have not been previously infected has been observed with Arzerra. Monitor patients for clinical and laboratory signs of hepatitis.

Progressive Multifocal Leukoencephalopathy[1]
Progressive multifocal leukoencephalopathy (PML) resulting in death has occurred with Arzerra. If PML is suspected, Arzerra should be discontinued and initiate evaluation for PML, including neurology consultation.

Tumor Lysis Syndrome[1]
Tumor lysis syndrome (TLS), including the need for hospitalization, has occurred in patients treated with Arzerra. Patients with high tumor burden and/or high circulating lymphocyte counts (>25 x 10^9/L) are at greater risk for developing TLS. Consider tumor lysis prophylaxis with anti-hyperuricemics and hydration beginning 12 to 24 hours prior to infusion of Arzerra. For treatment of TLS, administer aggressive intravenous hydration and anti-hyperuricemic agents, correct electrolyte abnormalities, and monitor renal function.

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Cytopenias[1]
Severe cytopenias, including neutropenia, thrombocytopenia, and anemia, can occur with Arzerra. Pancytopenia, agranulocytosis, and fatal neutropenic sepsis have occurred in patients who received Arzerra in combination with chlorambucil. Grade 3 or 4 late-onset neutropenia (onset at least 42 days after last treatment dose) and/or prolonged neutropenia (not resolved between 24 and 42 days after last treatment dose) were reported in patients who received Arzerra. Monitor complete blood counts at regular intervals during and after conclusion of therapy, and increase the frequency of monitoring in patients who develop Grade 3 or 4 cytopenias.

Immunizations[1]
The safety of immunization with live viral vaccines during or following administration of Arzerra has not been studied. The ability to generate an immune response to any vaccine following administration of Arzerra has not been studied.

Most Common Serious Adverse Reactions[1]
The following most common serious adverse reactions are discussed in greater detail above and in sections of the labeling: infusion reactions, hepatitis B virus reactivation, hepatitis B virus infection, progressive multifocal leukoencephalopathy, tumor lysis syndrome, cytopenias.

Most Common Adverse Reactions[1]
The most common adverse reactions (≥10%) seen in previously untreated CLL patients were infusion reactions and neutropenia. The most common adverse reactions (≥10%) seen in refractory CLL patients were neutropenia, pneumonia, pyrexia, cough, diarrhea, anemia, fatigue, dyspnea, rash, nausea, bronchitis and upper respiratory tract infections.

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.

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

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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

[1] ARZERRA Prescribing Information. January 2016.
[2] Chronic Lymphocytic Leukemia. Leukemia & Lymphoma Society Website. http://www.lls.org/#/diseaseinformation/leukemia/chroniclymphocyticleukemia/. Accessed April 8, 2014.
[3] What are the key statistics for chronic lymphocytic leukemia? American Cancer Society Website. http://www.cancer.org/cancer/leukemia-chroniclymphocyticcll/detailedguide/leukemia-chronic-lymphocytic-key-statistics. Published February 26, 2015. Accessed April 8, 2015.
[4] Veliz M, Pinilla-Ibarz J. Treatment of relapsed or refractory chronic lymphocytic leukemia. Cancer Control. 2012; 1:37-53.