GSK and Genmab Receive EU Authorization for Arzerra™ (ofatumumab) as First-Line Treatment for Chronic Lymphocytic Leukemia (CLL) in Combination with Chlorambucil or Bendamustine for Patients Ineligible for Fludarabine-based Therapy

Company Announcement

- **Arzerra approved for use in EU as first-line treatment for CLL in combination with chlorambucil or bendamustine for patients ineligible for fludarabine-based therapy**
- **Approval based on Phase III data from study with ofatumumab + chlorambucil & Phase II data from study with ofatumumab and bendamustine**

Copenhagen, Denmark; July 3, 2014 – GlaxoSmithKline plc (LSE: GSK) and Genmab A/S (OMX: GEN) announced today that the European Commission (EC) has granted marketing authorization for a new indication for the use of Arzerra™ (ofatumumab), a human monoclonal antibody against CD20, in combination with chlorambucil or bendamustine for the treatment of patients with chronic lymphocytic leukemia (CLL) who have not received prior therapy and who are not eligible for fludarabine-based therapy.[1]

"Today's decision by the European Commission for the first-line use of Arzerra offers a new treatment option for appropriate CLL patients and enables physicians flexibility in their choice of adjunct chemotherapy - chlorambucil or bendamustine," said Dr. Paolo Paoletti, President of Oncology, GSK.

"We are very pleased to receive this decision that Arzerra is approved in the EU in the front-line setting in combination with two different alkylating chemotherapies. This is another important milestone and we look forward to a successful launch under this new indication of the drug in Europe in the coming months. We hope to receive additional approvals in frontline across the globe in the future," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

The EC authorization of the first-line indication for Arzerra (ofatumumab) is based on results from two trials[1]:

- A randomized, Phase III open-label, parallel-arm, multicenter, pivotal study (OMB110911, COMPLEMENT 1) evaluating the combination of ofatumumab and chlorambucil (N=221) versus chlorambucil alone (N=226) in CLL patients for whom fludarabine-based treatment is considered inappropriate. In this study, treatment with ofatumumab and chlorambucil demonstrated a statistically significant, 71 per cent improvement in median progression-free survival (PFS) compared to chlorambucil alone (22.4 months versus 13.1 months, respectively) (HR=0.57 [95 per cent CI, 0.45, 0.72] p<0.001).[1]
- A single-arm, multicenter, Phase II study (OMB115991) evaluating ofatumumab in combination with bendamustine in 44 patients with previously untreated CLL for whom fludarabine-based treatment was considered inappropriate. Results of this study demonstrated that ofatumumab in combination with bendamustine provided an overall response rate (ORR) of 95 per cent [95 per cent CI, 85, 99] and a complete response rate (CR) of 43 per cent.[1]

Safety information for Arzerra (ofatumumab)
The overall safety profile of ofatumumab in CLL (previously untreated and relapsed or refractory) is based on data from 511 patients in clinical trials. This includes 250 patients with relapsed or refractory CLL who were treated with ofatumumab alone and 261 patients with previously untreated CLL for whom fludarabine-based therapy was considered inappropriate and who were treated in combination with an alkylating agent.

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).[1]

Contraindications:

Hypersensitivity to ofatumumab or to any of the excipients.[1]

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

Infusion reactions[1]

Ofatumumab has been associated with infusion reactions leading to temporary interruption of treatment or withdrawal of treatment. Infusion reactions may include anaphylactoid events, cardiac events, chills/rigors, cough, cytokine release syndrome, diarrhea, dyspnea, fatigue, flushing, hypertension, hypotension, nausea, pain, pyrexia, rash, and urticaria. 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 complications from severe reactions.

Tumor lysis syndrome[1]

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 (≥ 25,000/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[1]

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[1]

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[1]

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[1]

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 (i.e., >20 milliseconds) were detected.

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Bowel obstruction[1]
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.

Please consult the full Summary of Product Characteristics for all the labeled safety information for Arzerra.

About CLL

CLL, the most commonly diagnosed adult leukemia in Western countries,[2,3] accounts for approximately one-third of all cases of leukemia.[4] In Europe, the incidence rate for all subtypes of leukemia is 7.2 per 100,000 of which 34 per cent of cases are CLL, translating to approximately 12,500 new CLL cases each year.[5,6,7] Each year, CLL is responsible for approximately 6,000 deaths across Europe.[5,6,7] The average age of diagnosis is 72 years old,[4] and approximately 90 per cent of patients with CLL are estimated to be over the age of 55.[8] The majority of patients with CLL have at least one significant comorbidity such as hypertension, diabetes, cardiovascular disease, or chronic obstructive pulmonary disease (COPD).[9]

About ofatumumab

Arzerra (ofatumumab) is a monoclonal antibody that is designed to target the CD20 molecule found on the surface of CLL cells and normal B lymphocytes.[1]

Ofatumumab is also authorized in the EU 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.

Arzerra is a trademark of the GSK group of companies.

GSK – one of the world's leading research-based pharmaceutical and healthcare companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer. For further information please visit www.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 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.

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Forward Looking Statement for Genmab
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.

Genmab A/S and its subsidiaries own the following trademarks: Genmab®; the Y-shaped Genmab logo®; the DuoBody logo™; the Hexabody logo™; HuMax®; HuMax-CD20®; DuoBody®, HexaBody™ and UniBody®.

Cautionary statement regarding forward-looking statements
GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described under Item 3.D 'Risk factors' in the company's Annual Report on Form 20-F for 2013.

Registered in England & Wales:
No. 3888792

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References

1) GlaxoSmithKline. ARZERRA Summary of Product Characteristics 2014.
2) 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 27 May 2014.
3) Leukemia & Lymphoma Society. Chronic Lymphocytic Leukemia. http://www.lls.org/#/diseaseinformation/leukemia/chroniclymphocyticleukemia/. Accessed 27 May 2014.
4) 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 27 May 2014.
5) Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. http://globocan.iarc.fr. Accessed 3 June 2014.
6) United Nations. World Population Prospects, 2012 Revision. Population Division of the Department of Economic and Social Affairs, United Nations. http://esa.un.org/unpd/wpp/. Accessed February 2014.
7) Watson L, Wyld P, Catovsky D. Disease burden of chronic lymphocytic leukaemia within the European Union. Eur J Haematol 2008;81:253-258.
8) 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_6/vi50.full. Accessed 27 May 2014.
9) Shanafelt, TD, et al. Quality of life in chronic lymphocytic leukemia: an international survey of 1482 patients. British Journal of Hematology. 2007;139, 255-264.