GSK and Genmab Receive FDA Approval for Arzerra® (ofatumumab) as First-Line Treatment in Combination with Chlorambucil for Patients with Chronic Lymphocytic Leukemia (CLL) for Whom Fludarabine-Based Therapy is Considered Inappropriate

Company Announcement

- **Arzerra now approved for use in previously untreated patients for whom fludarabine-based therapy is considered inappropriate**
- **Approval based on Phase III data from study with ofatumumab + chlorambucil**

Copenhagen, Denmark; April 17, 2014 - GlaxoSmithKline plc (LSE: GSK) and Genmab A/S (OMX: GEN) announced today that the U.S. Food and Drug Administration (FDA) has approved a Supplemental Biologic License Application (sBLA) for the use of Arzerra® (ofatumumab), a CD20-directed monoclonal antibody, in combination with chlorambucil for the treatment of previously untreated patients with chronic lymphocytic leukemia (CLL) for whom fludarabine-based therapy is considered inappropriate. [1(p.1)]

The FDA approval of the first-line indication is based on results from a Phase III study (COMPLEMENT 1) which demonstrated statistically significant improvement in median progression-free survival (PFS) in patients who received the combination of ofatumumab and chlorambucil compared to patients who received chlorambucil alone.[1(p.16)]

"CLL is the most common form of leukemia amongst adults in Western countries, many of whom are elderly with multiple health issues," said Dr. Paolo Paoletti, President of Oncology, GSK. "Today's approval by the FDA for the use of Arzerra in the first-line setting means that appropriate patients with CLL have a new treatment option."

"We are pleased that Arzerra has been shown to provide clinical benefit and will now be available in the first-line setting. Arzerra, the first approved therapeutic created by Genmab and developed in collaboration with GSK, is the only therapeutic CD20 antibody approved in combination with chlorambucil for first-line CLL and as a monotherapy for CLL refractory to fludarabine and alemtuzumab," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab.

The results from COMPLEMENT 1, the randomized, open-label, parallel-arm, pivotal Phase III study evaluating the combination of ofatumumab and chlorambucil (N=221) versus chlorambucil alone (N=226) demonstrated statistically significant improvement in median PFS in patients randomized to ofatumumab and chlorambucil compared to patients randomized 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(p.16-17)]

The majority of adverse reactions (ARs) were Grade 2 or lower in both treatment arms. The most common (≥5 per cent in the ofatumumab plus chlorambucil arm and also ≥2 per cent more than in the chlorambucil monotherapy arm) non-infusion-related ARs (all grades) as reported by investigators within 60 days following the last treatment were neutropenia (27 per cent ofatumumab + chlorambucil, 18 per cent chlorambucil), asthenia (8 per cent, 5 per cent), headache (7 per cent, 3 per cent), leukopenia (6 per cent, 2 per cent), herpes simplex (6 per cent, 4 per cent), lower respiratory tract infection (5 per cent, 3 per cent), arthralgia (5 per cent, 3 per cent), and upper abdominal pain (5 per cent, 3 per cent).[1(p.9)]

Infusion reactions (IRs) were seen in 67 per cent of patients in the ofatumumab plus chlorambucil arm. Ten per cent of IRs were Grade 3 or greater. IRs that were Grade 3 or greater, serious or led to treatment interruption or discontinuation occurred most frequently with Cycle 1 and decreased with subsequent infusions.[1(p.9-10)]

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About CLL
CLL, the most commonly diagnosed adult leukemia in Western countries, [2(p.240), 3] accounts for approximately one-third of all cases of leukemia.[4] In the U.S., 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. [5(p.2),4] 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.[6] The majority of patients with CLL have at least one comorbidity such as hypertension, diabetes, cardiovascular disease, or COPD. [7(p.258-259)]

About COMPLEMENT 1
In the randomized, open-label, parallel-arm, pivotal Phase III COMPLEMENT 1 study, ofatumumab in combination with the oral chemotherapeutic agent chlorambucil versus chlorambucil alone was evaluated in 447 patients with CLL who were previously untreated and for whom fludarabine-based therapy was considered inappropriate by study investigators.[1(p.16)] Among the 447 patients (median age was 69 years) included in the study, the majority of patients (72 per cent) had 2 or more comorbidities.[1(p.16)]

The primary objective efficacy measure was PFS as assessed by a blinded Independent Review Committee (IRC) using the International Workshop for Chronic Lymphocytic Leukemia (IWCLL) updated National Cancer Institute-sponsored Working Group (NCI-WG) guidelines (2008).[1(p.16)] Secondary efficacy endpoints included overall response (OR), complete response (CR), and duration of response.[1(p.17)] The OR and CR rates were also assessed by an IRC.[1(p.17)]

With the exception of neutropenia and leukopenia, the overall rate of non-infusion-related Grade 3 or greater reactions with ofatumumab in combination with chlorambucil was similar to chlorambucil alone.[1(p.9)]

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 (p.2)]

- **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(p.6)]
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.

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Hepatitis B Virus Reactivation[1(p.6)]
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(p.7)]
Fatal infection due to hepatitis B in patients who have not been previously infected has been observed with Arzerra. Patients should be monitored for clinical and laboratory signs of hepatitis.

Progressive Multifocal Leukoencephalopathy[1(p.7)]
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(p.7)]
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 109/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.

Cytopenias[1(p.7-8)]
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(p.8)]
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(p.8)]
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.

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Most Common Adverse Reactions[1(p.8)]
The most common adverse reactions (≥10%) seen in previously untreated CLL patients were infusion reactions and neutropenia.

The revised full U.S. Prescribing Information, including Boxed Warning, will be available soon at https://www.gsksource.com/gskprm/htdocs/documents/ARZERRA.PDF. Prior to the revised label being posted online, a copy of the label may be requested from one of the GSK Media or Investor Relations contacts listed in the "GSK enquiries" section at the end of this document.

U.S. journalists, please click here for the U.S. electronic press kit: http://us.gsk.com/html/media-news/arzerra-press-kit.html.

About Arzerra (ofatumumab)
Arzerra (ofatumumab) is a CD20-directed monoclonal antibody indicated in combination with chlorambucil for the treatment of previously untreated patients with chronic lymphocytic leukemia (CLL) for whom fludarabine-based therapy is considered inappropriate.[1(p.1)]

Arzerra is also indicated as monotherapy for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.[1(p.1)]

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

Arzerra is a registered trademark of the GSK group of companies.

About GSK Patient Assistance Programs
GSK has a number of patient assistance programs for eligible patients in the United States who need help affording their medicines and vaccines. Patients who qualify for the programs may benefit from GSK's Commitment to Access program for oncology and specialty medicines which offers services and programs including co-pay assistance in addition to traditional patient assistance support. For more information, patients in the United States can call 1-8ONCOLOGY1 (1-866-265-6491).

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's first marketed antibody, ofatumumab (Arzerra®), was approved to treat chronic lymphocytic leukemia in patients who are refractory to fludarabine and alemtuzumab after less than eight years in development. Genmab's validated and next generation antibody technologies are expected to provide a steady stream of future product candidates. Partnering of 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.

Cautionary statement regarding forward-looking statements for GSK
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.

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