Genzyme Phase 3 Trial of Campath/Fludara Combination Shows Potential Benefit in Second-Line CLL

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Oral Presentation of Interim Data Given at the American Society of Hematology Annual Meeting

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Genzyme Corporation (Nasdaq: GENZ) announced data from its CAM314 randomized Phase 3 clinical trial comparing Campath® (alemtuzumab) in combination with Fludara® (fludarabine phosphate) (FluCAM) to Fludara alone in patients with relapsed and refractory chronic lymphocytic leukemia (CLL) demonstrated that the FluCAM regimen significantly reduced the risk of disease progression or death compared to single-agent Fludara. Importantly, advanced-stage, second-line CLL patients receiving FluCAM more than doubled the amount of time without disease progression in comparison to patients receiving Fludara alone. Data from the study were the subject of an oral presentation today at the 2009 Annual Meeting of the American Society of Hematology (ASH) in New Orleans, LA.

Based on the study’s positive preliminary findings, Genzyme intends to seek regulatory approvals to further broaden the Campath label to include the use of this combination regimen.

Following a planned second interim analysis, the CAM314 trial’s data safety monitoring panel recommended early closure of the study as it had achieved the pre-specified clinical and statistical significance in progression free survival (PFS), the study’s primary endpoint. While patients in the study continue to be followed, and final efficacy and safety data from the study are expected to be available in the second-half of 2010, response data from the second interim analysis (as assessed by the study’s investigators) reported at ASH indicate that the FluCAM combination provided significantly higher overall and complete response rates compared to Fludara alone. The preliminary results also suggest that the FluCAM regimen has an acceptable safety profile when compared to single-agent Fludara.

“The second interim analysis of the CAM314 data showed that the FluCAM regimen may offer significant benefits to patients with chronic lymphocytic leukemia in first relapse,” said study principal investigator and ASH presenter Andreas Engert, MD, Professor of Internal Medicine, Hematology and Oncology, University Hospital of Cologne, Germany. “The FluCAM regimen also had a dosing schedule that was more convenient for patients and physicians.”

“There are limited published randomized trial data evaluating treatment regimens specifically in the second-line setting for patients with chronic lymphocytic leukemia, contributing to the wide variability in treatment patterns seen in this setting,” said Cyndi Sirard, MD, Medical Director, Genzyme Transplant and Oncology, and an author of the study. “The CAM314 trial advances our understanding of how to use Campath in combination with Fludara and may offer an alternative to existing regimens used in this setting.”

With a median of 17 months of follow up at the time of the second interim analysis, and as assessed by the independent data safety monitoring panel (IRRP), the FluCAM arm demonstrated superior progression free survival in comparison to Fludara alone, with median PFS of 29.6 months on the FluCAM regimen compared to 20.7 months for patients on Fludara, reducing the risk of disease progression or death by 39 percent (p=0.005). Of particular note, in the pre-specified subgroup of patients with advanced, Rai stage III-IV CLL, the median PFS was 26.1 months for FluCAM and 12.1 months for Fludara (p=0.003).

In addition, according to clinical trial investigator assessments, the FluCAM regimen provided significantly higher overall and complete response rates. The overall response rate of patients on FluCAM was 84.8 percent compared to 67.9 percent on Fludara (p=0.001). The complete response rate was 30.4 percent on FluCAM versus 16.4 percent on Fludara (p=0.002).

An additional secondary endpoint, overall survival, did not reach significance at this interim analysis.

Safety Information

The FluCAM combination regimen provided a lower total exposure to both Campath (50 percent reduction) and Fludara (30 percent reduction) compared to the labeled, single-agent dosing regimen for each drug in CLL.

Deaths occurring on therapy or within 30 days after last dose were two percent in the FluCAM arm versus five percent in the Fludara arm.

Serious adverse events occurred in 33 percent of patients in the FluCAM arm compared to 26 percent of patients in the Fludara arm. Grade 3 and 4 infections were 10.4 percent in the FluCAM arm and 9.1 percent in the Fludara arm. Symptomatic
CMV infection occurred only in the FluCAM arm in 8 percent of patients, of which one percent was considered an SAE. No CMV infection in the FluCAM arm was classified as greater than grade 3.

Adverse events (AEs) occurring in more than 10 percent of patients in both arms included neutropenia, thrombocytopenia, anemia, and leukopenia. Treatment-emergent grade 3/4 hematologic shifts revealed a frequency of thrombocytopenia (18 percent vs. 22 percent), neutropenia (60 percent vs. 66 percent) and anemia (13 percent vs. 22 percent) which were comparable in the FluCAM and Fludara arms respectively. Additional AEs in more than 10 percent of patients in the FluCAM arm, but not the Fludara arm, included pyrexia, chills, lymphopenia, rash, infusion related reactions, nausea and urticaria.

Chronic lymphocytic leukemia is the most common type of leukemia in adults, accounting for approximately 25-30 percent of all forms of leukemia. The median age of patients diagnosed with CLL is 72 years. While CLL is generally considered a disease that is slow to progress, it remains incurable and most patients will eventually require a second-line treatment option.

Genzyme has established a leading position in therapies to manage hematological malignancies. The company has expanded its commercial presence in the field by acquiring the sales and marketing rights to Campath, Fludara and Leukine® (sargramostim). Genzyme also markets Clolar ® (clofarabine injection), known as Evolitra® in Europe, and Mozobil® (plerixafor injection), two important therapies for managing patients with certain types of blood cancers.

About the CAM314 Phase 3 Study

The CAM314 Phase 3 study was a multicenter, international, open-label, randomized study that included 335 patients with progressive Rai stage I-IV chronic lymphocytic leukemia, as defined by the 1996 National Cancer Institute Working Group criteria. The study investigated whether treatment of patients with relapsed or refractory CLL with FluCAM was more beneficial than treatment with Fludara alone. Patients in the trial received one prior therapy, and excluded patients who were refractory to Fludara or Campath. FluCAM patients received Campath in escalating doses of 3, 10, 30 mg IV (days 1-3 up to 14 days). The patients then received Fludara at 30 mg/m² IV (days 1-3) followed by Campath 30 mg IV (days 1-3) every 28 days for up to 6 cycles. Patients in the Fludara arm received Fludara at 25 mg/m² IV daily for 5 consecutive days (days 1-5) every 28 days for up to 6 cycles. The primary endpoint was progression-free survival. Secondary endpoints included overall response, complete response, safety, and overall and three year survival.

About Campath (alemtuzumab)

Alemtuzumab is a humanized monoclonal antibody that binds to a specific target, CD52, on cell surfaces and directs the body's immune system to destroy those cells. It is the first and only monoclonal antibody approved by the FDA for the treatment of patients with B-CLL.

Campath for B-CLL has a boxed warning that includes information on cytopenias, infusion reactions, and infections. The most commonly reported adverse reactions in patients with B-CLL were infusion reactions (fever, chills, hypotension, urticaria, nausea, rash, tachycardia, dyspnea), cytopenias (neutropenia, lymphopenia, thrombocytopenia, anemia), and infections (CMV viremia, CMV infection, other infections). Other commonly reported adverse reactions include vomiting, abdominal pain, insomnia and anxiety. The most commonly reported serious adverse reactions are cytopenias, infusion reactions, and immunosuppression/infections.

About Fludara (fludarabine phosphate)

Fludara, a purine nucleotide analog, inhibits the synthesis of new DNA, thus preventing leukemia cells from multiplying. Fludara for injection should be administered under the supervision of a qualified physician experienced in the use of antineoplastic therapy. Fludara for injection can severely suppress bone marrow function. When used at high doses in dose-ranging studies in patients with acute leukemia, Fludara for injection was associated with severe neurologic effects, including blindness, coma, and death. This severe central nervous system toxicity occurred in 36% of patients treated with doses approximately four times greater (96 mg/m²/day for 5-7 days) than the recommended dose. Similar severe central nervous system toxicity has been rarely (≤ 0.2%) reported in patients treated at doses in the range of the dose recommended for chronic lymphocytic leukemia.

Instances of life-threatening and sometimes fatal autoimmune hemolytic anemia have been reported to occur after one or more cycles of treatment with Fludara for injection. Patients undergoing treatment with Fludara for injection should be evaluated and closely monitored for hemolysis.

In a clinical investigation using Fludara for injection in combination with pentostatin (deoxycoformycin) for the treatment of refractory chronic lymphocytic leukemia (CLL), there was an unacceptably high incidence of fatal pulmonary toxicity. Therefore, the use of Fludara for injection in combination with pentostatin is not recommended.

Fludara is contraindicated in those patients who are hypersensitive to this drug or its components. The most common adverse events include myelosuppression (neutropenia, thrombocytopenia and anemia), fever and chills, infection, and nausea and vomiting. Other commonly reported events include malaise, fatigue, anorexia, and weakness. Serious opportunistic infections have occurred in CLL patients treated with Fludara.

About Genzyme

One of the world's leading biotechnology companies, Genzyme is dedicated to making a major positive impact on the lives of people with serious diseases. Since 1981, the company has grown from a small start-up to a diversified enterprise with more than 11,000 employees in locations spanning the globe and 2008 revenues of $4.6 billion.

With many established products and services helping patients in nearly 100 countries, Genzyme is a leader in the effort to develop and apply the most advanced technologies in the life sciences. The company's products and services are focused on rare inherited disorders, kidney disease, orthopaedics, cancer, transplant and immune disease, and diagnostic testing. Genzyme's commitment to innovation continues today with a substantial development program focused on these fields, as
well as cardiovascular disease, neurodegenerative diseases, and other areas of unmet medical need.

This press release contains forward-looking statements regarding Genzyme’s future plans and business strategies, including without limitation, statements about the potential uses and benefits of the FluCAM combination, expectations for when final data will become available, and Genzyme’s plans to seek regulatory approval for Campath in combination use with Fludara. These statements are subject to risks and uncertainties that could cause actual results to differ materially from those projected in these forward-looking statements, including: the actual efficacy and safety of the FluCAM combination; the timing and outcome of discussions with the regulatory agencies regarding approval of Campath for combination use with Fludara; and the risks and uncertainties described in reports filed by Genzyme with the Securities and Exchange Commission under the Securities Exchange Act of 1934, as amended, including without limitation the information under the heading “Risk Factors” in Genzyme’s Quarterly Report on Form 10-Q for the quarter ending September 30, 2009. Genzyme cautions investors not to place substantial reliance on the forward-looking statements contained in this press release.

These statements speak only as of the date of this press release, and Genzyme undertakes no obligation to update or revise these statements.

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