FDA Approves Rituxan Plus Chemotherapy for the Most Common Type of Adult Leukemia

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-- Approval Based on Data From Two of the Largest Trials Ever Conducted in Chronic Lymphocytic Leukemia --

SOUTH SAN FRANCISCO, Calif. & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Genentech, Inc., a wholly owned member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), and Biogen Idec (Nasdaq: BIIB) announced today the U.S. Food and Drug Administration (FDA) approved Rituxan®(rituximab) in combination with fludarabine and cyclophosphamide (FC) for people with previously untreated and previously treated CD20-positive chronic lymphocytic leukemia (CLL).

CLL is the most common form of adult leukemia and is a slow growing cancer that occurs when abnormal or malignant white blood cells are found in the blood and bone marrow. Because it is considered incurable, a primary goal of treatment is to increase the length of time patients live without the disease worsening (progression-free survival or PFS).

“Rituxan with chemotherapy can delay the need for additional treatment because it significantly extends the time people with CLL live without the disease worsening,” said Hal Barron, M.D., executive vice president, Global Development and chief medical officer, Roche and Genentech. “This approval provides an important option and new hope to the many people with this incurable cancer.”

“This approval in CLL reinforces the importance of Rituxan in hematologic cancers,” said Greg Reyes, M.D., Ph.D., senior vice president, Oncology Research and Development, Biogen Idec. “We are very pleased that Rituxan, either alone or in combination, has now achieved its fifth approval for the most common forms of non-Hodgkin’s lymphoma and adult leukemia.”

According to the American Cancer Society, there are nearly 90,000 people in the United States living with CLL, accounting for one-third of all leukemia cases. In 2009, more than 15,000 new CLL cases were expected to be diagnosed in the U.S.

Rituxan Efficacy in CLL

The approval is based on data from two Phase III studies, CLL8 and REACH. Sponsored by Roche and conducted by the German CLL Study Group, CLL8 was a global, multi-center, randomized, open-label, Phase III study that enrolled 817 patients with previously untreated CD20-positive CLL. REACH was a global, multi-center, randomized, open-label, Phase III study sponsored by Genentech, Biogen Idec and Roche that enrolled 552 patients with previously treated CD20-positive CLL who had not previously received Rituxan (Rituxan-naïve). Both studies evaluated Rituxan plus FC compared with FC alone. The primary endpoint for both studies was PFS and secondary endpoints included overall survival, event-free survival, duration of response, response rate, complete response and toxicity.

Previously Untreated CLL: CLL8

- In CLL8, previously untreated patients who received Rituxan plus FC had a 79 percent improvement in the time patients lived without their disease getting worse compared to those who received FC alone (based on a 44 percent risk reduction, a hazard ratio of 0.56, p<0.01; 95 percent confidence interval: 0.43, 0.71).
- Patients who received Rituxan plus FC lived a median of 39.8 months without the disease worsening compared to 31.5 months for patients who received FC alone.
- The PFS results were supported by significant increases in both overall and complete response rates.

Previously Treated CLL: REACH

- In REACH, previously treated Rituxan-naïve patients who received Rituxan plus FC had a 32 percent improvement in the time patients lived without their disease getting worse compared to those who received FC alone (based on a 24 percent risk reduction, a hazard ratio of 0.76, p=0.02; 95 percent confidence interval: 0.60, 0.96).
- Previously treated patients who received Rituxan plus FC lived a median of 26.7 months without the disease worsening compared to 21.7 months for patients who received FC alone.
- The PFS results were supported by significant increases in both overall and complete response rates.

In people with CLL aged 70 or older, exploratory analyses suggest there was no benefit with the addition of Rituxan to FC. Patients 70 years or older received lower dose intensity of fludarabine and cyclophosphamide compared to younger patients, regardless of the addition of Rituxan.

Rituxan Safety in CLL

No new safety signals were observed in either CLL8 or REACH and safety was consistent overall with previous Rituxan experience. Severe (Grade 3 or greater) adverse events that occurred more frequently in patients who received Rituxan plus FC compared to those who received FC alone included cytopenias (neutropenia, leukopenia, febrile neutropenia, thrombocytopenia, pancytopenia), infusion-related reactions and, in previously untreated patients, hypotension and hepatitis B. The incidence of Grade 3 or 4 infections in previously untreated and previously treated CLL patients was similar for both study arms for the overall study populations. For patients who received Rituxan plus FC, the incidence of Grade 3 and 4 adverse events was higher in those older than 70 years of age compared with younger patients.

About Rituxan

Rituxan is a therapeutic antibody that binds to a specific protein called CD20 found on the surface of cancerous and normal B-cells. In non-Hodgkin’s lymphoma (NHL) and rheumatoid arthritis (RA), Rituxan works with the body’s own immune system to eliminate marked CD20-positive B-cells. Stem

cells (B-cell progenitors, those cells that give rise to B-cells) in bone marrow do not have the CD20 protein. B-cells usually regenerate after Rituxan treatment and return to normal levels in about 12 months for most patients.

Rituxan, discovered by Biogen Idec, first received FDA approval in November 1997 for the treatment of relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent. It was approved in the European Union under the trade name MabThera® in June 1998. Rituxan is also approved for the treatment of NHL for the following:

- Previously untreated follicular, CD20-positive, B-cell NHL in combination with CVP chemotherapy.
- Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent, after first-line CVP chemotherapy.
- Previously untreated diffuse large B-cell, CD20-positive, NHL in combination with CHOP (or other anthracycline-based chemotherapy regimens).

Rituxan received FDA approval for RA in February 2006 and is currently indicated in combination with methotrexate for the treatment of adult patients with moderately- to severely-active RA who have had inadequate response to one or more tumor necrosis factor antagonist therapies. Rituxan is not recommended for use in patients with severe active infections.

Genentech and Biogen Idec co-market Rituxan in the U.S., and Roche markets MabThera in the rest of the world, except Japan, where Rituxan is co-marketed by Chugai and Zenyaku Kogyo Co., Ltd.

Rituxan Safety

Rituxan therapy can result in serious side effects, some which can be life-threatening.

These include **infusion reactions, tumor lysis syndrome (TLS), severe mucocutaneous reactions, progressive multifocal leukoencephalopathy (PML),** hepatitis B infection that may become active again, other infections, heart problems, serious kidney problems and serious stomach and bowel problems.

The most common side effects of Rituxan in clinical trials of patients with CLL were side effects from the infusion and low blood cell counts. Most side effects from the infusion happened within 24 hours of the start of the infusion, and included nausea, fever, chills, low blood pressure, vomiting and difficulty breathing.

Most people experienced at least one serious side effect. CLL patients who were older than 70 years of age had more serious side effects compared to patients 70 or younger. The most frequently reported serious side effect was low blood cell counts.

Patients should read the Rituxan Full Prescribing Information including Boxed WARNINGS, and the Medication Guide at http://www.rituxan.com.

About Genentech Access Solutions

Genentech is committed to people having access to our medicines. Genentech Access Solutions is a team of 350 Genentech employees who help those who need Genentech medicines. This team works with patients and doctors to resolve reimbursement and insurance issues and provides assistance to eligible patients in the United States who do not have insurance coverage or who cannot afford their out-of-pocket co-pay costs.

Since its first medicine was approved in 1985, Genentech has donated approximately $1.5 billion in free Genentech medicines to the uninsured through the Genentech® Access to Care Foundation (GATCF) and other product donation programs. The household income limit to receive free medicine through GATCF is $100,000 per year. Since 2005, Genentech has also donated approximately $390 million to various independent, non-profit organizations that provide financial assistance to those who cannot access needed medical treatment due to co-pay costs.

About Genentech

Founded more than 30 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines to treat patients with serious or life-threatening medical conditions. The company, a wholly owned member of the Roche Group, has headquarters in South San Francisco, Calif. For additional information about the company, please visit http://www.gene.com.

About Biogen Idec

Biogen Idec creates new standards of care in therapeutic areas with high unmet medical needs. Founded in 1978, Biogen Idec is a global leader in the discovery, development, manufacturing, and commercialization of innovative therapies. Patients worldwide benefit from Biogen Idec's significant products that address diseases such as lymphoma, multiple sclerosis, and rheumatoid arthritis. For product labeling, press releases and additional information about the company, please visit http://www.biogenidec.com.

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