Chugai Pharmaceutical Co., Ltd.
Nippon Shinyaku Co., Ltd.

New Drug Application Filed for Glycoengineered Type II Anti-CD20 Monoclonal Antibody, Obinutuzumab

TOKYO, August 23, 2017 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) and Nippon Shinyaku Co., Ltd. (TOKYO: 4516) announced today that Chugai filed a new drug application to the Ministry of Health, Labour and Welfare (MHLW), for glycoengineered type II anti-CD20 monoclonal antibody, obinutuzumab (genetical recombination) which was co-developed by the two companies for the treatment of “CD20-positive B-cell follicular lymphoma (FL)” in Japan.

"Combination therapy of rituximab and chemotherapy has been used as the standard treatment for CD20-positive B-cell FL for a long time. As a new treatment option, Obinutuzumab was confirmed to be more beneficial than the conventional treatment with rituximab for the treatment of FL," said Dr. Yasushi Ito, Chugai’s Senior Vice President, Head of Project & Lifecycle Management Unit. "We are committed to deliver obinutuzumab to patients as early as possible to contribute to the access to better treatments in Japan."

Dr. Kazuya Mori, Nippon Shinyaku's Corporate Officer, Head of R&D Administration Div. said "I am very glad that a new drug application for our co-developed product, obinutuzumab, was filed. By adding this new product to our lineup in the area of hematologic malignancies, on which we are focusing, we will make utmost efforts to meet the demands of the clinical setting and contribute to the treatment of patients."

This filing was based on the results of the GALLIUM study, a global phase III clinical study conducted by Roche and participating from Japan and other several clinical studies.
The GALLIUM study is a global Phase III open-label, multi-center, randomized two-arm study that evaluated the efficacy and safety of obinutuzumab plus chemotherapy followed by obinutuzumab alone (obinutuzumab arm) compared with rituximab plus chemotherapy followed by rituximab alone (rituximab arm) in 1,401 patients with previously untreated CD20-positive advanced non-Hodgkin’s lymphoma. The primary endpoint of the study was investigator-assessed progression free survival (PFS) in 1,202 patients with FL. The secondary endpoints were PFS assessed by an independent review committee (IRC), overall survival (OS), safety, and other endpoints.

With respect to the primary endpoint, as the median PFS was not reached, the results showed that obinutuzumab arm reduced the risk of disease progression, recurrence or death in patients with FL by 34 percent (HR=0.66, 95% CI: 0.51-0.85, p=0.0012, stratified log-rank test, Data cut-off: January 31, 2016) compared to rituximab arm. Concerning secondary endpoints, the median PFS assessed by the IRC was not reached as well, the risk of disease progression, recurrence or deaths decreased by 29% (HR=0.71, 95% CI: 0.54-0.93], p=0.0138, stratified log-rank test, Data cut-off: January 31, 2016). The median OS did not reach in both arms due to small numbers of events. As

for safety, the adverse events (AEs) expressed in both arms in the GALLIUM study were consistent with previous reports. The Grade 3 or higher AEs which was observed in 5% or more frequently for obinutuzumab arm than rituximab arm was neutropenia (43.9% for obinutuzumab arm vs. 37.9% for rituximab arm).

Obinutuzumab is a glycoengineered type II anti-CD20 monoclonal antibody designed to attach to CD20, a protein expressed on certain B cells, but not on stem cells or plasma cells, same as rituximab which is recommended as a treatment of non-Hodgkin's lymphoma in treatment guidelines in Japan and overseas. Obinutuzumab is designed to attack and destroy targeted B-cells both directly and together with the body's immune system.

In Japan, the prevalence of malignant lymphoma was reported to be approximately 27,000 and the number of deaths due to the disease was reported to be approximately 11,000 in 2012[1, 2]. Since the cases of Hodgkin's lymphoma is reported to account for approximately 8 to 10% of the cases of malignant lymphoma in Japan[3], the prevalence of non-Hodgkin's lymphoma is estimated to be approximately 24,000 and the number of deaths from this condition is estimated to be approximately 10,000. The prevalence of and deaths from malignant lymphoma tend to increase in recent years[1, 2], and a same tendency is seen in patients with non-Hodgkin's lymphoma.

Chugai and Nippon Shinyaku will work for the early approval to provide obinutuzumab as a new treatment option for patients with CD20-positive B-cell follicular lymphoma and medical professionals.

1. Center for Cancer Control and Information Services, National Cancer Center. National estimates of cancer incidence based on cancer registries in Japan (1975-2012) (http://ganjoho.jp/en/)
2. Center for Cancer Control and Information Services, National Cancer Center. Cancer mortality from Vital Statistics in Japan (1958-2015) (http://ganjoho.jp/en/)
3. Japanese Society of Hematology. Guidelines on Treatment of Hematopoietic Tumors (2013) Version 1.2. (http://www.jshem.or.jp/gui-hemali/table.html, Japanese only)

Contacts	
Chugai Pharmaceutical Co., Ltd. Corporate Communications Dept. Media Relations Group Tel : +81-(0)3-3273-0881	Nippon Shinyaku Co., Ltd. Corporate Communications Dept. Tel : +81-(0)75-321-9103