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

# Filing of Humanized Anti-CD20 Monoclonal Antibody Gazyva for Additional Indication of Chronic Lymphocytic Leukemia

*Chugai files for regulatory approval following the results from the* Phase III ELEVATE-TN *study evaluating Gazyva and acalabrutinib in patients with untreated CLL*

TOKYO, March 7, 2022 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) and Nippon Shinyaku Co., Ltd. (TOKYO: 4516) announced that Chugai filed a regulatory application with the Ministry of Health, Labour and Welfare (MHLW), for approval of an anti-cancer agent/humanized anti-CD20 monoclonal antibody Gazyva® Intravenous Infusion 1000 mg [generic name; obinutuzumab (genetical recombination)] for the treatment of chronic lymphocytic leukemia (CLL).

“Ensuring safety during long-term treatment is increasingly important as the recent expansion in treatment options may lead to longer survival for patients with CLL. As a result, there is a growing unmet medical need for treatments that control disease and have an acceptable safety profile,” said Chugai’s President and CEO, Dr. Osamu Okuda. “We are working towards approval of Gazyva so the drug can contribute to treatment as a new therapeutic option for CLL.”

“We are very pleased that Gazyva was applied for marketing approval for a new indication in CLL,” said Nippon Shinyaku's President, Toru Nakai. “We believe that the addition of the CLL indication to Gazyva will help medical needs and further contribute to the treatment of patients in the field of hematologic malignancies, which is one of our focus field.”

The filing is based on the results including Phase III ELEVATE-TN study (ACE-CL-007) conducted by AstraZeneca, evaluating the efficacy and safety of Gazyva and acalabrutinib (Bruton's tyrosine kinase (BTK) inhibitor, brand name Calquence®) in patients with untreated CLL.

**About ELEVATE-TN study**

ELEVATE-TN (ACE-CL-007, NCT02475681) study is a randomized, multicenter, open-label Phase III trial evaluating the safety and efficacy of acalabrutinib in combination with obinutuzumab or alone versus chlorambucil (unapproved) in combination with obinutuzumab in previously untreated patients with CLL. In the study, patients are randomized 1:1:1 to following groups;

- Chlorambucil plus obinutuzumab
- Acalabrutinib plus obinutuzumab
- Acalabrutinib monotherapy

The primary endpoint is IRC-assessed progression-free survival (PFS) with acalabrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab. Secondary endpoint is IRC-assessed PFS with acalabrutinib monotherapy versus chlorambucil plus obinutuzumab. Other secondary endpoints are objective response rate, time to next treatment and overall survival etc [1)].

**About Gazyva (obinutuzumab)**
Gazyva is a glycoengineered type II anti-CD20 monoclonal antibody designed to bind to CD20, a protein expressed on certain B cells, but not on stem cells or plasma cells. Gazyva is designed to attack and destroy targeted B cells both directly and together with the body's immune system. Chugai and Nippon Shinyaku jointly develop and market the product in Japan.

**About chronic lymphocytic leukemia (CLL)**
Chronic lymphocytic leukemia (CLL) a rare type of lymphoma accounting for less than one case in 100,000 population annually [2)]. In CLL, blood stem cells in the bone marrow become excessive abnormal lymphocytes and these abnormal cells have difficulty fighting infections. As the number of abnormal cells grows there is less room for healthy white blood cells, red blood cells, and platelets. This could result in anemia, infection, and bleeding [3)]. B-cell receptor signaling through BTK is one of the essential growth pathways for CLL.



[Reference]
1. ClinicalTrials.gov. Elevate CLL TN: Study of Obinutuzumab + Chlorambucil, Acalabrutinib (ACP-196) + Obinutuzumab, and Acalabrutinib in Subjects With Previously Untreated CLL. https://clinicaltrials.gov/ct2/show/NCT02475681 [Internet. Accessed in January 2022]
2. Center for Cancer Control and Information Services, National Cancer Center. Chronic lymphocytic leukemia/small lymphocytic lymphoma https://ganjoho.jp/public/cancer/CLL/index.html [Internet. Accessed in January 2022. Japanese only]
3. Takizawa J, et al. Comparative Analysis of Japanese and European Typical CLL Patients. Blood. 02 December 2016;128(22):5564.

| Contacts | |
|---|---|
| Chugai Pharmaceutical Co., Ltd.<br>Corporate Communications Dept.<br>Media Relations Group<br>Tel: +81-(0)3-3273-0881<br>Investor Relations Group<br>Tel: +81-(0)3-3273-0554 | Nippon Shinyaku Co., Ltd.<br>Corporate Communications Dept.<br>Tel: +81-(0)75-321-9103 |