CHUGAI

Roche Roche Group

News Release

Preclinical Results of the Anti-CTLA-4 Switch Antibody ROSE12 Published in the Journal for ImmunoTherapy of Cancer

- Preclinical results of ROSE12, an anti-CTLA-4 switch antibody engineered with Chugai's proprietary Switch-Ig technology, have been accepted by the Journal for ImmunoTherapy of Cancer, a leading journal in cancer immunotherapy
- ROSE12 binds to CTLA-4 (Cytotoxic T-Lymphocyte Antigen-4) in an adenosine triphosphate (ATP)-dependent manner and depletes regulatory T cells (Tregs) within tumors, suggesting the potential to enhance tumor-selective immune responses
- Phase I clinical study in solid tumors is currently underway

TOKYO, January 28, 2026 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that the preclinical study results of ROSE12, an anti-CTLA-4 switch antibody discovered by Chugai and currently being evaluated in a Phase I clinical study in patients with solid tumors, have been published in the Journal for ImmunoTherapy of Cancer. The Journal for ImmunoTherapy of Cancer is a prestigious academic journal in the field of cancer immunotherapy, published by the Society for Immunotherapy of Cancer (SITC).

"ROSE12, a novel anti-CTLA-4 FcγRs binding-enhanced antibody activated by extracellular adenosine triphosphate, shows tumor selective regulatory T-cell depletion and antitumor efficacy without systemic immune activation"
https://jitc.bmj.com/content/14/1/e013397

This study demonstrated the following:

- ROSE12, an anti-CTLA-4 antibody that binds to CTLA-4 in an ATP-dependent manner and selectively depletes Tregs in tumors where ATP is present at high concentrations, was discovered
- ROSE12 binds to CTLA-4 in the presence of ATP, exhibits antibody-dependent cellular cytotoxicity (ADCC) activity, and depletes Tregs. In contrast, ROSE12 does not bind to CTLA-4 or exhibit activity in the absence of ATP (*in vitro* studies)
- ROSE12 demonstrated antitumor efficacy in mouse models bearing multiple cancer cell lines, including those resistant to existing immune checkpoint inhibitors (mouse studies)
- ROSE12 reduced systemic immune reactions mediated by mechanisms such as Treg depletion in normal tissues (mouse studies)
- ROSE12 was confirmed to be tolerable in toxicity studies using monkeys

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1 Nihonbashi-Muromachi 2-chome, Chuo-ku, Tokyo 103-8324 Japan
Media Relations Group TEL: +81-(0)3-3273-0881 E-mail: pr@chugai-pharm.co.jp
Investor Relations Group TEL: +81-(0)3-3273-0554 E-mail: ir@chugai-pharm.co.jp

About ROSE12
ROSE12 is an anti-CTLA-4 switch antibody utilizing Chugai's proprietary antibody engineering technology, Switch-Ig. It is designed to recognize adenosine triphosphate (ATP), which is known to be present at high concentrations in tumor tissues, as a switch molecule to become activated and selectively deplete regulatory T cells (Tregs) that highly express CTLA-4. Phase I clinical study in patients with solid tumors is currently underway to demonstrate that ROSE12 exerts antitumor efficacy while avoiding systemic immune-related adverse events through its tumor-selective mechanism of action.
ROSE12 was discovered using Chugai's drug discovery technologies, originating from the joint research project with Professor Shimon Sakaguchi, Distinguished Honorary Professor of the University of Osaka and Specially Appointed Professor at the Immunology Frontier Research Center (IFReC), a leading authority in Treg research.

About Switch-Ig
Switch-Ig is a technology that enhances the disease site selectivity of antibodies. Conventional antibodies can bind to target antigens not only at disease sites but also in normal tissues, potentially causing problems such as adverse events. Switch-Ig antibodies are designed to bind to target antigens in the presence of molecules (switch molecules) that are selectively present at high concentrations at disease sites, and are less likely to react with target antigens in normal tissues where the concentration of switch molecules is low. By using this technology, antibodies can be made to react selectively at disease sites, which is expected to reduce toxicity issues caused by binding to normal tissues.

About Regulatory T Cells (Tregs)
Tregs play a central role in immune suppression and are one of the important target cells in cancer immunotherapy. The primary role of Tregs is to regulate the activity of other immune cells. For example, they suppress excessive immune responses. However, reduced Treg function can disrupt the balance of the immune system, potentially leading to autoimmune diseases, such as IPEX syndrome*, rheumatoid arthritis, type-1 diabetes, and multiple sclerosis. Conversely, overactive Tregs can suppress antitumor immune responses, potentially worsening cancer[1].

*IPEX syndrome: A syndrome involving immune abnormalities caused by mutations in FOXP3. IPEX stands for immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome. Patients with IPEX syndrome present with severe allergies, autoimmune thyroid disorders, type 1 diabetes, and inflammatory bowel disease.

Switch-Ig mentioned in this release is protected by law.

Sources
1. Wadell, C.M. et al.：Harnessing the biology of regulatory T cells to treat disease. Nat Rev Drug Discov., 24(2), 93-111 (2025)

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