



Antagonistic Antibody Targeting TNFR2 Inhibits Regulatory T Cell Function to Promote Anti-Tumor Activity

Yonglin Chen, Manxue Jia, Sharon Wang, Sherry Xu and Nanhai He*

Department of Biosciences, Adlai Nortye USA Inc., North Brunswick, NJ, United States

NEW JERSEY and HANGZHOU, China, recently – Adlai Nortye Ltd. ("Adlai Nortye"), a clinical-stage biopharmaceutical company focused on the development of innovative cancer therapies, announced the publication of preclinical research of AN3025 (anti-hTNFR2) in the peer-reviewed journal *Frontiers in Immunology*.

The article entitled "Antagonistic Antibody Targeting TNFR2 Inhibits Regulatory T Cell Function to Promote Anti-Tumor Activity" is authored by Dr. Nanhai He, Head of Drug Discovery of Adlai Nortye, and his colleagues including Dr. Yonglin Chen, Dr. Manxue Jia, Sharon Wang and Dr. Sherry Xu. In this study, Dr. He and his team presents the preclinical results of in-vitro and in-vivo characterization of AN3025, an anti-TNFR2 antibody with great potentials in the field of immunotherapy. Observations include but are not limited to the followings:

- AN3025 treatment can reduce the proportion of regulatory T cells (Treg), increase the infiltration of effector CD4+ T cells and CD8+ T cells, and upregulate the expression of immune activation genes such as interferon- γ (IFN- γ) and granzyme K (Granzyme K) in the tumor microenvironment, leading to strong anti-tumor effects.
- AN3025 monotherapy significantly inhibits tumor growth both in PD-1-sensitive MC38 and in PD-1-resistant B16F10 animal tumor models.
- The combination of AN3025 and a PD-1 inhibitor shows superior anti-tumor effect than monotherapies preclinically.

The corresponding author, Dr. Nanhai He, Head of Drug Discovery of Adlai Nortye, stated, "Our internally developed TNFR2 antagonist antibody, dubbed AN3025, has demonstrated encouraging anti-tumor activities in animal models, and we are committed to pushing this exciting project through preclinical evaluation and looking forward to its clinical development in the near future."

The leading author of the article, Dr. Yonglin Chen, Scientist of Adlai Nortye, added, "Immune checkpoint inhibitors (ICIs) are important milestones of modern immunotherapy and have been approved for treatment of various human tumors. However, not all the patients respond to ICIs and moreover, many patients develop acquired resistance to ICIs afterwards. The exploration of new targets and new treatments, has become increasingly important in the field of cancer immunotherapy. The TNFR2 antagonizing antibody AN3025 has shown great potentials for tumor control in preclinical studies, and we are very much looking forward to the clinical development of AN3025."

About TNFR2

TNFR2 is a member of the tumor necrosis factor receptor superfamily (TNFRSF) and is highly expressed on the surface of regulatory Treg cells in the tumor microenvironment. Mechanistically, TNFR2 plays a key role in maintaining Treg cell proliferation, stability and activation, and the TNFR2-expressing Treg cells are considered to be the most immunosuppressive Treg population. Therefore, TNFR2 has been proposed to be one of the most promising Treg targets in cancer immunotherapy.

About AN3025 (anti-hTNFR2)

AN3025 is a novel humanized IgG1 antibody that recognizes human TNFR2 and is currently in preclinical development. The antibody binds to the extracellular domain of human TNFR2 with sub-nanomolar affinity and blocks the downstream signaling pathway of TNFR2 by preventing TNFR2 from binding to its ligand TNF. AN3025 effectively inhibits Treg cells in the tumor microenvironment and enhances the anti-tumor immune response. In both PD-1-sensitive and PD-1-resistant animal tumor models, AN3025 monotherapy shows vigorous anti-tumor activities. The combination of AN3025 and a PD-1 inhibitor demonstrates superior antitumor effects to monotherapies in preclinical studies.

About Adlai Nortye

Adlai Nortye is a clinical-stage biopharmaceutical company focused on the development of innovative cancer therapies, with its R&D centers in both China and the U.S. With a strategic emphasis on oncology, the Company has built a global pipeline through collaborations and internal discovery with more than 10 drug candidates in development. Currently, four of them are being investigated in multiple clinical trials, including (i) Buparlisib(AN2025) which received the FDA Fast-Track designation and was in a global Phase III clinical trial; (ii) Pelareorep (AN1004), an intravenously delivered oncolytic virus which received the FDA Fast-Track designation and have completed a phase II clinical trial; (iii) Palupiprant (AN0025), an oral EP4 antagonist which has completed Phase Ib trial in a neoadjuvant setting in localized advanced rectal cancer and is undergoing Phase Ib trial in combination with Keytruda® in patients with multiple solid tumors; and (iv) AN4005, an orally available, small molecule PD-L1 inhibitor which was currently in Phase Ia trial that was shown to functionally overcome the inhibition derived from PD-1/L1 interaction in reporter- and human PBMC (hPBMC)-based cellular assays. In addition, Adlai Nortye also completed the first patient dosing for its Phase I clinical trial in collaboration with Roche to evaluate the triple combination of AN2025, AN0025 and Tecentriq® (PD-L1 inhibitor) for a variety of PIK3CA mutant solid tumors in September 2021 in the U.S.

Adlai Nortye has assembled an experienced management team, built its proprietary immuno-oncology platforms and partnered with multiple top pharmaceutical companies to promote innovation. Adlai Nortye is committed to becoming an innovative biopharmaceutical company with global vision and strives to benefit patients worldwide. The mission of the Company is to transform deadly cancer into a chronic and eventually a curable disease. For more information, please visit: www.adlainortye.com.