Antengene Presents Four Posters at AACR 2025 Highlighting Focuses on AnTenGager™ TCEs and Synthetic Lethality

Shanghai and Hong Kong, PRC, April 26, 2025 — Antengene Corporation Limited ("**Antengene**" , SEHK: 6996.HK), a leading innovative, commercial-stage global biopharmaceutical company dedicated to discovering, developing and commercializing first-in-class and/or best-in-class medicines for hematologic malignancies and solid tumors, today announced that **it has released results from four preclinical studies in poster presentations at the 2025 American Association for Cancer Research Annual Meeting (AACR 2025). These four posters feature Antengene's four highly differentiated and high-potential programs, including ATG-201 (CD19 x CD3 TCE) and ATG-042 (MTAP^{null}-selective PRMT5 Inhibitor), which are poised to enter clinical development in the second half of 2025; ATG-110 (LY6G6D x CD3 TCE), which was developed on the AnTenGager™ TCE 2.0 platform for the treatment of microsatellite stable colorectal cancer; and a companion diagnostic antibody developed to assess CD24 expression and guide clinical studies of CD24-targeted therapies.**

Details of the Poster Presentations:

ATG-201 (CD19 x CD3 T cell engager)

Title: ATG-201, a novel T-cell engager (TCE) effectively depletes B cells with reduced risk of CRS for the treatment of B cell malignancies and B cell related autoimmune diseases

Abstract Number: 7326

Session Category: Immunology

Session Title: T Cell Engagers and Novel Antibody-Based Therapies

Date: April 30, 2025

Time: 9:00 AM - 12:00 PM (Central Time)

10:00 PM, April 30, 2025 - 1:00 AM, May 1, 2025 (Beijing Time)

Location: Poster Section 40

- **Introduction:** By depleting autoreactive B cells, CD19-targeted CAR-T have shown early yet promising efficacy in treating patients with B cell-driven autoimmune diseases. However, the clinical application of TCE continues to be greatly hindered by the unfavorable pharmacokinetics and toxicity associated with cytokine release syndrome. To overcome these limitations, Antengene developed ATG-201, a "2+1" CD19 x CD3 TCE, which was evaluated in a series of *in vitro* studies for binding affinity, T cell dependent cytotoxicity (TDCC) cytokine release, and drug developability. The *in vivo* anti-lymphoma efficacy and pharmacodynamic effect were evaluated in Raji xenograft model. The tissue resident B cell depletion was assessed in CD34+ hematopoietic stem cells humanized mice. Pharmacokinetic parameters of ATG-201

were evaluated in normal Balb/c mice.

- **Results:** ATG-201 demonstrated high affinity binding to CD19, limited T cell binding before CD19 crosslinking, highly potent CD19-dependent T cell cytotoxicity against CD19+ B cells, as well as enhanced naïve B cell depletion with reduced cytokine release compared to clinical benchmarks. In lymphoma models, the study observed potent *in vivo* efficacy with reduced cytokine release. In CD34+ hematopoietic stem cells humanized mice, ATG-201 was able to induce complete B cell depletion with reduced cytokine release. ATG-201 has a mAb-like pharmacokinetic profile in wild type mice and good drug developability. Moreover, surrogate CD19 x CD3 AnTenGager TCE displayed potent efficacy in MRL/lpr spontaneous systemic lupus erythematosus (SLE) mouse models and MOG-Induced EAE models.
- **Conclusions:** ATG-201 demonstrated CD19-dependent CD3 binding and activation, inducing effective B cell depletion *in vitro* and *in vivo* with low cytokine release, which provides potential for the treatment of B cell malignancies and B cell related autoimmune diseases. ATG-201 is poised to enter clinical development in the second half of 2025.

ATG-042 (MTAP^{null}-selective PRMT5 Inhibitor)

Title: Preclinical characterization of ATG-042, a novel MTAP^{null}-selective PRMT5 inhibitor

Abstract Number: 4230

Session Category: Experimental and Molecular Therapeutics

Session Title: HDAC and Methyltransferase Inhibitors

Date: April 29, 2025

Time: 9:00 AM - 12:00 PM (Central Time)

10:00 PM, April 29, 2025 - 1:00 AM, April 30, 2025 (Beijing Time)

Location: Poster Section 16

- **Introduction:** Targeting the PRMT5-MTA complex has become a promising strategy for treating MTAP^{null} cancer in a synthetically lethal manner, avoiding on-target-off-tumor hematological toxicity when using first-generation, non-selective PRMT5 inhibitors. Herein, Antengene developed ATG-042, a novel MTAP^{null}-selective PRMT5 small molecule inhibitor with good brain penetration. In this study, the *in vitro* activity and MTAP selectivity of ATG-042 were profiled using HCT116 MTAP wild type (wt) cells, HCT116 MTAP knock out (ko) cells and multiple endogenous MTAP^{null} cell lines. The *in vivo* efficacy was tested in cell derived xenograft (CDX) mouse models with HCT116 MTAP wt cells, HCT116 MTAP ko cells, LU99 cells (MTAP^{null}) and U87MG-luc (MTAP^{null}). The pharmacokinetic and toxicological properties were assessed with corresponding assay methods.
- **Results:** ATG-042 showed excellent anti-proliferative activities on multiple endogenous MTAP^{null} cell lines with IC_{50} values between 10nM

and 100nM. ATG-042 demonstrated high permeability, good metabolic stability, and low risk of drug-drug interaction. *In vivo* PK study shows that ATG-042 is well absorbed, with a dose-dependent increase in plasma distribution and high oral bioavailability in mice, SD rats and beagle dogs. Furthermore, ATG-042 is brain-penetrable (B/P ratio=51% in mice; $KPuu_{brain}$=0.73 in rats). ATG-042 showed robust *in vivo* efficacy in both subcutaneous CDX models (HCT116 -MTAP ko, LU99) and orthotopic CDX model (U87MG-luc) as a single agent. In addition, ATG-042 also exhibited potential synergy in combination with other drugs for antitumor therapy.

- **Conclusions:** ATG-042 is an oral $MTAP^{null}$-selective PRMT5 inhibitor with potent efficacy against $MTAP^{null}$ tumor. It also demonstrated good tolerability and brain penetrability. ATG-042 is poised to enter clinical development in the second half of 2025.

ATG-110 (LY6G6D x CD3 T cell engager)

Title: ATG-110, a novel "2+1" LY6G6D-targeted T-cell Engager (TCE) with high potency for the treatment of MSS colorectal cancer

Abstract Number: 3509

Session Category: Immunology

Session Title: T Cell Engagers

Date: April 28, 2025

Time: 2:00 PM - 5:00 PM (Central Time)

3:00 AM - 6:00 AM, April 29, 2025 (Beijing Time)

Location: Poster Section 38

- **Introduction:** Colorectal cancer (CRC) is one of the most common cancers worldwide and requires more effective and safer therapies to improve the poor survival outcome, particularly in patients with microsatellite stable (MSS) colorectal cancer, who exhibit primary resistance to immune checkpoint inhibitors and lack effective treatment options. T cell engagers have shown encouraging efficacy in treating hematological malignancies, while exhibiting suboptimal clinical efficacies in solid tumors. The risk of cytokine release syndrome (CRS) remains as a significant challenge clinically. ATG-110 is a novel "2+1" LY6G6D x CD3 TCE developed by Antengene. In this study, ATG-110 was evaluated in a series of preclinical *in vitro* studies for binding affinity, T cell activation and cytokine release, T cell dependent cytotoxicity (TDCC), and drug developability. The *in vivo* anti-tumor efficacy was evaluated in PBMC-humanized immunodeficient NDG mice engrafted with LY6G6D^{medium}-expression HT55 or LY6G6D$^{very\ low}$-expression SW480 MSS CRC cells.
- **Results:** ATG-110 binds to LY6G6D-positive cell lines, including LY6G6D-overexpression 293T and HT55 with the nanomolar grade EC_{50}. The CD3 binding site of ATG-110 is concealed by the LY6G6D Fab arm

before binding to LY6G6D, due to the steric hindrance. Therefore, ATG-110 demonstrated limited binding capability to CD3+ cells before LY6G6D crosslinking. It activates T cells and induces cytokine release only in the presence of LY6G6D+ cells. *In vitro*, ATG-110 resulted in potent T cell dependent cytotoxicity with single-digit pM IC_{50} values on HT55 cells. ATG-110 also showed highly potent *in vitro* efficacy against $LY6G6D^{low}$-expression cells. ATG-110 exhibited a low risk of inducing cytokine release syndrome. ATG-110 demonstrated potent anti-tumor activity in PBMC-humanized HT55 xenograft model. Furthermore, ATG-110 also demonstrated good drug developability.

- **Conclusions:** ATG-110 demonstrated LY6G6D-dependent CD3 binding and activation with low risk of CRS. It showed powerful *in vitro* and *in vivo* anti-tumor efficacy against colorectal cancer, which warrants further clinical evaluation.

ATG-1144 (CD24 CDx Antibody)

Title: Development of a diagnostic antibody for CD24 targeted therapy

Abstract Number: 671

Session Category: Clinical Research

Session Title: Diagnostic Biomarkers 2

Date: April 27, 2025

Time: 2:00 PM - 5:00 PM (Central Time)

3:00 AM - 6:00 AM, April 28, 2025 (Beijing Time)

Location: Poster Section 29

- **Introduction:** CD24 has emerged as a promising therapeutic target for anti-cancer treatment. Several clinical trials are being conducted to evaluate the safety and efficacy of CD24-targeted therapies. Here, Antengene developed and characterized an anti-CD24 diagnostic antibody to enhance the screening and selection of patients based on CD24 expression. In this study, the authors described the discovery of the diagnostic antibody, and the evaluation of accuracy, sensitivity (selectivity), specificity, and assay precision of the antibody.
- **Results:** Monoclonal antibody clone ATG-1144 binds to the hCD24 core peptide in ELISA with an EC_{50} of 0.06 nM. Distinct membrane staining on human normal esophageal tissue FFPE specimens can also be observed with IHC staining using ATG-1144. For accuracy assessment, six CDX and twenty human specimens, comprising both positive and negative specimens (including solid tumors and B-cell non-Hodgkin lymphomas), were validated. Samples exhibiting high, medium, and low CD24 expression levels were evaluated for sensitivity and specificity, and the interpreted results aligned with the reference outcomes. FFPE tissues from three distinct patients were evaluated for assay precision assessment. The TMA IHC staining result revealed that 50-80% of patients with lung, breast, bladder, ovarian, or liver cancer have CD24

expression on tumor cell surface with low expression in the para-cancerous normal tissue.

- **Conclusions:** ATG-1144 specifically binds to human CD24 with high sensitivity as demonstrated by IHC staining. The development and validation of the method have been finalized using Leica Bond III platforms. These data suggest a potential diagnostic use of ATG-1144 for identifying CD24+ patients.

About Antengene

Antengene Corporation Limited (**"Antengene"**, SEHK: 6996.HK) is a leading commercial-stage R&D-driven global biopharmaceutical company focused on the discovery, development, manufacturing and commercialization of innovative first-in-class/best-in-class therapeutics for the treatment of hematologic malignancies and solid tumors, in realizing its vision of **"Treating Patients Beyond Borders"**.

Antengene has built a pipeline of 9 oncology assets at various stages going from clinical to commercial, including 6 with global rights, and 3 with rights for the APAC region. To date, Antengene has obtained 31 investigational new drug (IND) approvals in the U.S. and Asia, and submitted new drug applications (NDAs) in 11 Asia Pacific markets, with the NDA for XPOVIO® (selinexor) already approved in Mainland of China, Taiwan China, Hong Kong China, Macau China, South Korea, Singapore,

Malaysia, Thailand, Indonesia and Australia.

Forward-looking statements

The forward-looking statements made in this article relate only to the events or information as of the date on which the statements are made in this article. Except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, after the date on which the statements are made or to reflect the occurrence of unanticipated events. You should read this article completely and with the understanding that our actual future results or performance may be materially different from what we expect. In this article, statements of, or references to, our intentions or those of any of our Directors or our Company are made as of the date of this article. Any of these intentions may alter in light of future development. For a further discussion of these and other factors that could cause future results to differ materially from any forward-looking statement, please see the other risks and uncertainties described in the Company's Annual Report for the year ended December 31, 2024, and the documents subsequently submitted to the Hong Kong Stock Exchange.