ALPHAMAB ONCOLOGY

康寧傑瑞生物製藥

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 9966)

VOLUNTARY ANNOUNCEMENT

RESEARCH UPDATES OF JSKN021 AND JSKN022 FOR PRESENTATION AT 2025 AACR ANNUAL MEETING

This announcement is made by Alphamab Oncology (the "**Company**", together with its subsidiaries, the "**Group**") on a voluntary basis to inform the shareholders (the "**Shareholders**") and potential investors of the Group about the latest business advancement of the Group.

The board (the "**Board**") of directors (the "**Directors**") of the Company is pleased to announce that the research updates on preclinical activities of JSKN021 and JSKN022, have been presented during a poster session (abstract presentation number: 5450 and 5451) at the 2025 AACR Annual Meeting, which is held from April 25 to April 30, 2025. Such research results are summarized as below.

PHARMACOLOGICAL ACTIVITY OF JSKN021 IN PRECLINICAL STUDIES

Background: EGFR and HER3, both belonging to the EGFR family, are widely overexpressed in human malignancies, rendering them promising targets for cancer treatment. Cancer is a heterogeneous disease. Inter-and intratumor heterogeneity is believed to be a major factor contributing to recurrence, metastasis and resistance to current SOCs. To address these therapeutic challenges, the Company generated JSKN021, a dual payload ADC targeting EGFR/HER3. Both payloads, a novel DNA topoisomerase I inhibitor (T01, Alphatecan) and MMAE, are conjugated to glycan on Fc via cleavable linkers. The conjugation processes were carried out via combination of glycan transferase and click reaction. The streamlined process generated site specific and homogeneous conjugation with DAR4 (T01, Alphatecan) and DAR2 (MMAE). In this study, the pharmacological activity of JSKN021 was evaluated using relevant in vitro cell killing assays and in vivo models.

Methods: A novel TOPO1 inhibitor T01, Alphatecan and MMAE were stably conjugated to an EGFR/HER3 mAb using a glycan based site-specific manner. The conjugated products were characterized by LC-MS. Binding specificity of JSKN021 was confirmed by ELISA. In addition, release of payload was evaluated by LC-HRMS. At last, in vitro cell growth inhibitory and in vivo antitumor activities of JSKN021 were evaluated using different cancer cell lines and CDX models in comparison to single payload ADCs.

Results: After conjugation, LC-MS results showed that JSKN021 had a homogeneous DAR4 for T01 payload and DAR2 for MMAE. JSKN021 was demonstrated to bind EGFR and HER3 simultaneously. In addition, both T01 and MMAE were detected in cell culture supernatant and suspension of HCC827. Yet, no other metabolites were found detectable. JSKN021 demonstrated excellent stability in rats, mice, monkeys, and human serum, with minimal payload release. The stability was derived from the advantage of glycan based conjugation. JSKN021 inhibited the growth of cancer cells with either HER3 or EGFR or both expression, such as HCC827, MDA-MB-468, A431 and NCI-H1975. Furthermore, JSKN021 showed stronger tumor inhibition efficacy than mono payload ADCs in multiple CDX models.

PHARMACOLOGICAL ACTIVITY OF JSKN022 IN PRECLINICAL STUDIES

Background: mAb targeting PD-1/PD-L1 have significantly transformed cancer therapy. However, the majority of patients still cannot get benefit from this treatment or may develop resistance afterwards. The increased expression of PD-L1 in tumors makes it an attractive target for ADC development leading to the most advanced program in registration trials. The Company developed a multi-specific ADC targeting another set of antigens, ITGB6/8. Integrins are cell surface receptors that usually mediate cell to cell adhesion. Integrin β6/8 (ITGB6/8), which can only form a heterodimer with the αv integrin subunit, is highly expressed in various tumors. Utilizing our proprietary site-specific glycan conjugation, we generated JSKN022, an innovative PD-L1/ITGB6/8 targeting ADC, which structurally composed of a sdAb (single domain antibody) Fc fusion protein targeting PD-L1 and ITGB6/8, a cleavable linker and a novel DNA topoisomerase I inhibitor (T01, Alphatecan). In this study, the pharmacological activity of JSKN022 was evaluated using preclinical in vitro and in vivo models.

Methods: Based on Envafolimab, we designed a novel sdAb-Fc fusion protein which targeting both PD-L1 and ITGB6/8. Then T01 was homogeneously and stably conjugated to glycan located on Fc. The conjugated product (DAR4) was thoroughly characterized by LC-MS. The binding specificity of JSKN022 and its internalization rate were assessed. Pattern of payload released were analyzed using LC-HRMS. Serum stability was tested across various species. In vitro cell growth inhibition and in vivo antitumor efficacy of JSKN022 were examined using a range of cancer cell lines and CDX models with parental antibody ADC as control.

Results: JSKN022 demonstrated specific binding to the αvβ6/8 protein, without cross-reactivity with other members of integrin family. JSKN022 exhibited a consistent DAR4. Bridging ELISA indicated that JSKN022 can simultaneously bind to both PD-L1 and ITGB6/8. Flow cytometry binding assays revealed that JSKN022 possessed a superior binding capacity compared to both parental antibodies. Correspondingly, the naked antibody of JSKN022 showed an increased internalization rate relative to parental antibodies in HCC4006 and Capan-2 tumor cells. JSKN022 effectively inhibits the proliferation of antigen-positive cancer cells and exhibited enhanced tumor suppression compared to the single-target ADCs. Furthermore, benefiting from glycan conjugation, JSKN022 demonstrated excellent stability in serum from rats, mice, monkeys, and humans, with minimal T01 release.

ABOUT JSKN021

JSKN021 is a first-in-class dual payload ADC consisting of an EGFR/HER3 bispecific antibody conjugated with novel TOPO1 inhibitor (T01) and MMAE. Engineered with finely tuned binding avidity in both arms to address tumor heterogeneity while minimizing on-target, off-tumor toxicity, JSKN021 was designed for enhanced stability and improved homogeneity. It combines T01 (DAR 4) and MMAE (DAR 2) payloads to overcome non-response and resistance observed with single-payload treatment strategies.

ABOUT JSKN022

JSKN022 is a first-in-class multi-specific ADC targeting both PD-L1 and αVβ6, integrating IO mechanisms with ADC approaches. This novel therapeutic utilizes glycan-specific conjugation for precise payload attachment, delivering the proprietary TOPO1 inhibitor Alphatecan via a cleavable linker to enhance stability and efficacy. Clinical evaluations confirm the clinical feasibility of this approach, with preliminary data indicating no significant safety concerns associated with its unique targeting mechanism.

ABOUT THE COMPANY

The Company is a leading biopharmaceutical company in China with a fully integrated proprietary technology platform in ADCs, bispecific antibodies and multifunctional protein engineering. The Company's highly differentiated in-house pipeline consists of ADCs, mAb and bispecific antibodies in staggered development status in oncology, including, among others, one product approved for marketing by the NMPA and multiple products in phase III or pivotal clinical trial stages. The Company has developed various technologies and platforms of antibody-based therapies for oncology treatment and expertise in this regard. Benefitting from the proprietary protein engineering platforms and structure-guided molecular modeling expertise, the Company is able to create a new generation of multi-functional biological drug candidates that could potentially benefit patients globally.

DEFINITIONS AND GLOSSARY OF TECHNICAL TERMS

"2025 AACR Annual Meeting"	the 2025 annual meeting of American Association for Cancer Research, one of the first and largest cancer research organizations dedicated to accelerating the conquest of cancer
"ADC(s)"	antibody-drug conjugate(s)
"Alphatecan"	Alphamab's proprietary linker-payload system comprising a novel topoisomerase inhibitor, T01
"CDX"	cell line-derived xenograft, a model used for the research and testing of anti-cancer therapies. Human tumor samples are cultured as cell lines and implanted into mouse models to test the efficacy of antitumor compounds *in vivo*
"China"	the People's Republic of China
"DAR"	drug-to-antibody ratio, refers to the average number of drug molecules that are attached to each antibody molecule
"DNA"	Deoxyribonucleic Acid
"ELISA"	the enzyme-linked immunosorbent assay, a commonly used analytical biochemistry assay
"EGFR"	epidermal growth factor receptor

"Fc"	fragment crystallizable region, which is the tail region of an antibody that interacts with cell surface receptors called Fc receptors and some proteins of the complement system
"HER3"	human epidermal growth factor receptor 3
"*in vitro*"	studies using components of an organism that have been isolated from their usual biological surroundings, such as microorganisms, cells or biological molecules
"*in vivo*"	studies in which the effects of various biological entities are tested on whole, living organisms as opposed to a partial or dead organism, or those done *in vitro*
"IO"	immuno-oncology
"ITGB6/8"	Integrin Beta-6/8
"LC-HRMS"	liquid chromatography-high resolution mass spectrometry
"LC-MS"	liquid chromatography-mass spectrometry
"mAb"	monoclonal antibody
"MMAE"	Monomethyl auristatin E
"NMPA"	National Medical Products Administration of China (國家藥品監督管理局)
"PD-1"	Programmed Cell Death Protein 1
"PD-L1"	Programmed Death-Ligand 1
"sdAb"	single domain antibody
"TOPO1"	topoisomerase I
"αVβ6"	Alpha-V Beta-6 integrin
"SOCs"	Standards of Care
"%"	per cent

Cautionary Statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited: The Company cannot guarantee that it will be able to develop and/or ultimately market JSKN021 and JSKN022 successfully. Shareholders and potential investors of the Company are advised to exercise due care when dealing in the shares of the Company.

By Order of the Board
Alphamab Oncology
Dr. XU Ting
Chairman and Executive Director

Hong Kong, April 30, 2025

As at the date of this announcement, the Board comprises Dr. XU Ting as the chairman of the Board and executive Director and Ms. LIU Yang as executive Director, Mr. CHO Man as non-executive Director, and Dr. GUO Zijian, Mr. WEI Kevin Cheng and Mr. WU Dong as independent non-executive Directors.