**ALPHAMAB ONCOLOGY**

**康寧傑瑞生物製藥**

*(Incorporated in the Cayman Islands with limited liability)*

**(Stock Code: 9966)**

# VOLUNTARY ANNOUNCEMENT

# PRESENTATION OF RESEARCH UPDATES ON KN046 AND KN026 AT THE SABCS 2022

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

The board of directors of the Company (the "**Board**") announces that three phase II clinical trial results have recently been released at the SABCS 2022: (i) the research results of a phase II clinical trial of KN046 in combination with nab-paclitaxel in mTNBC; (ii) the research results of a phase II clinical trial of KN026 in combination with docetaxel as the first-line treatment for HER2-positive recurrent or metastatic BC; and (iii) the preliminary results of a phase II clinical trial of KN026 in combination with docetaxel as neoadjuvant treatment for HER2-positive early or locally advanced BC. The e-posters have been presented at SABCS 2022, which will also be presented at the Company's website at http://www.alphamabonc.com, correspondingly.

## EFFICACY, SAFETY AND TOLERABILITY OF KN046 (AN ANTI-PD-L1/CTLA-4 BISPECIFIC ANTIBODY) IN COMBINATION WITH NAB-PACLITAXEL IN MTNBC: FINAL RESULTS OF THE PHASE II TRIAL

This phase II clinical trial is designed to evaluate the efficacy, safety and tolerability of KN046 in combination with nab-paclitaxel for the treatment of mTNBC. This clinical trial enrolled patients with treatment-naïve locally advanced inoperable or metastatic TNBC. The eligible patients received nab-paclitaxel and KN046 in two cohorts with different dose levels (Cohort A and Cohort B). Cohort A patients received KN046 at 3mg/kg Q2W and Cohort B patients received KN046 at 5mg/kg Q2W. Tumor response was evaluated Q8W according to RECIST v1.1. The primary endpoints included ORR evaluated by the independent review committee, and the secondary endpoints included PFS, OS, safety and tolerability.

As of August 21, 2022, the date of data cut-off, 27 patients were enrolled, among whom, 16 patients were assigned into Cohort A and 11 patients were assigned into Cohort B. The median age of all enrolled patients was 50 years old (range: 33 to 70 years old) and 24 patients (88.9%) were at stage IV. The median follow-up was 27.93 months (IQR: 20.73 to 30.46).

- *Efficacy.* For 25 patients evaluable for efficacy, the ORR was 44.0% (95% CI: 21.1 to 61.3), DCR was 96.0% (95% CI: 79.6 to 99.9) and CBR was 52.0% (95% CI: 31.3 to 72.2). The DoR was 11.9 months (95% CI: 5.59 to NE). The median PFS was 7.33 months (95% CI: 3.68 to 11.07), and among the PD-L1≥1% patients, the median PFS was 8.61 months (95% CI: 1.61 to NE). The median OS is immature, the preliminary result of which is 27.73 months (95% CI: 14.75 to NE), and the 2-year OS rate was 60.1% (95% CI: 37.2 to 76.9). Both PD-L1 positive and negative patients derived OS benefit from the combination treatment.

- *Safety.* Patients tolerated well to the combination therapy in this trial. 13 patients (48.1%) experienced irAEs, and only 3 (11.1%) were at grade 3 and higher levels. The incidence rate of SAE was 33.3%. The most commonly (≥20%) TRAEs at grade 3 and higher levels include neutrophil count decreased (9 patients, 33.3%) and white blood cell count decreased (8 patients, 29.6%), and there was no treatment-related death.

**Conclusions**: The combination therapy of KN046 plus nab-paclitaxel has shown favorable clinical efficacy in mTNBC, especially in PD-L1 positive patients. By the date of data cut-off, the median OS is not mature and there is still more than half of patients alive, which demonstrated an encouraging 2-year OS rate. Patients in this trial tolerated well to the combination therapy and safety profile was manageable.

**EFFICACY AND SAFETY RESULTS OF KN026, A HER2 BISPECIFIC ANTIBODY COMBINED WITH DOCETAXEL IN FIRST-LINE TREATMENT OF HER2-POSITIVE RECURRENT/METASTATIC BREAST CANCER**

The preliminary safety and efficacy results of a phase I clinical trial of KN026 monotherapy in HER2-positive advanced BC were presented at the 2020 ASCO annual meeting, showing a promising efficacy and well-tolerated safety. The phase II clinical trial results of KN026 combined with docetaxel are presented below.

This clinical trial enrolled eligible patients with HER2-positive and first-line systemic treatment-naïve recurrent or metastatic BC. Patients received KN026 at 30mg/kg Q3W in combination with docetaxel at 75mg/m$^2$ Q3W until disease progression, unacceptable toxicity, or other circumstances that require drug discontinuation. The primary endpoints were ORR and DoR, and the secondary endpoints included PFS, OS and safety.

As of August 18, 2022, the date of data cut-off, 57 female patients were enrolled, and the median follow-up was 16.6 months (95% CI：15.15 to 19.29). Among all enrolled patients, the median age was 52 years old, and 52 (91.2%) patients were at stage IV.

- *Efficacy.* For 55 patients evaluable for efficacy, the confirmed ORR was 76.4% (95% CI: 62.98 to 86.77) and DoR was 24.0 months (95% CI: 18.07 to NE). The DCR was 100% (95% CI: 93.51 to 100). The median PFS was 25.4 months (95% CI: 16.53 to NE) and the median PFS is immature. The median OS was not reached and the 12-month, 18-month and 24-month OS rates were 93.0% (95% CI: 82.37 to 97.31), 91.2% (95% CI: 80.05 to 96.22), and 91.2% (95% CI: 80.05 to 96.22), respectively.

- *Safety.* The incidence rates of treatment adverse event at grade 3 and higher levels and SAE associated with KN026 were 38.6% (22/57) and 8.8% (5/57), respectively. The incidence rate of SAE was 15.8% (9/57), including 3 (5.3%) patients for febrile neutropenia, 2 (3.5%) patients for white blood cell count decreased and less than 2% for other SAEs. There was no death due to KN026 drug-related adverse events in the clinical trial.

**Conclusions**: KN026 in combination with docetaxel is well tolerated and has shown promising clinical benefit as a first-line treatment for HER2-positive advanced BC. As of the date of data cut-off, the median PFS was 25.4 months, and 24-month OS rate was 91.2%, which demonstrated encouraging efficacy results and significant long-term survival benefits.

**KN026 IN COMBINATION WITH DOCETAXEL AS NEOADJUVANT TREATMENT FOR HER2-POSITIVE EARLY OR LOCALLY ADVANCED BREAST CANCER: A SINGLE-ARM, MULTI-CENTER, PHASE II STUDY**

This is a single-arm, multi-center, phase II clinical trial designed to evaluate the efficacy and safety of KN026 in combination with docetaxel as neoadjuvant treatment of HER2-positive early or locally advanced BC. Patients with treatment-naïve HER2-positive early or locally advanced BC were enrolled to receive 4 cycles of KN026 (30mg/kg, Q3W) and docetaxel (75mg/m$^2$, Q3W) neoadjuvant treatment. The primary endpoint was the tpCR rate. The secondary endpoints were bpCR rate, ORR, safety, PK and immunogenicity.

As of September 10, 2022, the date of data cut-off, all 30 patients were enrolled, among whom, 16 (53.3%) patients were at stage II, 14 (46.7%) patients were at stage III; 26 (86.7%) patients with lymph node metastases, and 4 (13.3%) patients without lymph node metastases; 15 (50.0%) patients were hormone receptor positive, and 15 (50.0%) patients were hormone receptor negative.

- *Efficacy.* Among 20 patients who completed the surgery and pathological evaluation, the tpCR rate was 50% (10/20, 95% CI: 27.20 to 72.80), the bpCR rate was 55% (11/20, 95% CI: 31.53 to 76.94) and the ORR was 100% (20/20, 95% CI: 83.16 to 100).

- *Safety.* The incidence rate of SAEs at grade 3 and higher levels was 6.7% (2/30). The incidence rate of KN026-related SAE was 3.3% (1/30), and no patient experienced severe cardiac toxicity.

**Conclusions**: KN026 in combination with docetaxel as neoadjuvant treatment has shown promising clinical benefit for patients with HER2-positive early or locally advanced BC with an acceptable and manageable safety profile.

**ABOUT KN046**

KN046 is a global innovative PD-L1/CTLA-4 bispecific antibody independently developed by the Group, targeting both PD-L1 and CTLA-4 with a clear structural differentiation to improve localization with the tumor microenvironment and to reduce off-target toxicity. Approximately 20 clinical trials of KN046 in different stages covering more than 10 types of tumors including NSCLC, TNBC, esophageal squamous cell carcinoma, hepatocellular carcinoma, pancreatic ductal adenocarcinoma and thymic carcinoma have been conducted in China, the United States of America and Australia. The results of these clinical trials have demonstrated a preliminary profile of good safety and promising efficacy of KN046. Among them, the preliminary results of phase II clinical trials in China indicate promising activity of KN046 for NSCLC, pancreatic ductal adenocarcinoma, hepatocellular carcinoma and TNBC as a single therapy and in combination therapy with chemotherapy. The Group has published preliminary promising safety and efficacy data of KN046 in patients who have failed prior treatments with immune checkpoint inhibitors. The Group has initiated two pivotal clinical trials in NSCLC, a pivotal clinical trial in pancreatic ductal adenocarcinoma and a pivotal trial in thymic carcinoma. The Group is also exploring cooperation opportunities to conduct clinical trials of KN046 in combination with its business partners' drug candidates, to achieve better therapeutic effects.

The preclinical and clinical trial results of KN046 have shown promising efficacy and indicated that KN046 is able to significantly reduce toxicity to human peripheral system. The Company believes that KN046 has the potential to become a breakthrough in cancer immunotherapy.

**ABOUT KN026**

KN026 was designed to be a global-level next-generation HER2-targeted therapy. With its innovative structure, it binds simultaneously to 2 distinct clinically validated epitopes of HER2 (paratope II and IV), and maintains a wild type Fc region. This results in (i) a dual blockade of HER2-related signaling pathways, (ii) strengthened binding to HER2 receptors, (iii) a reduction of HER2 proteins on the cell surface, and (iv) increased tumor killing effect through intact antibody-dependent cell-mediated cytotoxicity. These binding mechanisms enable KN026 to have excellent tumor suppressive effect. Several phase I/II clinical trials of KN026 have shown good preliminary efficacy in patients with advanced HER2-positive breast cancer and GC/GEJ. Currently, the pivotal clinical trial of KN026 combined with chemotherapy in patients with HER2-positive GC (including GEJ) who have failed first-line treatment is ongoing in China.

**ABOUT THE COMPANY**

The Company is a leading biopharmaceutical company in China with a fully integrated proprietary biologics platform in bispecific and protein engineering. Differentiated in-house clinical pipeline of the Company includes the oncology drug candidates with one approved for marketing by the NMPA, three in late clinical stage and two in phase I clinical trial stage. 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 new drug candidates that could potentially benefit patients globally.

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| "95% CI" | 95% confidence interval, a commonly used concept in biostatistics, meaning in approximately 95 out of 100 times, the interval will contain the true mean value |
| "2020 ASCO annual meeting" | the 2020 annual meeting of American Society of Clinical Oncology |
| "BC" | breast cancer |
| "bpCR" | breast pathologic complete response |
| "CBR" | clinical benefit rate |
| "CTLA-4" | cytotoxic T-lymphocyte-associated protein 4 |
| "DCR" | disease control rate |
| "docetaxel" | a chemotherapy medication used to treat a number of types of cancer |
| "DoR" | duration of response |
| "GC" | gastric cancer |
| "GEJ" | gastroesophageal junction cancer |
| "HER2" | human epidermal growth factor receptor 2 |
| "HER2-positive" | HER2 IHC 3+ or HER2 gene amplification |
| "IHC" | immunohistochemistry, which tests whether or not the cancer cells have HER2 receptors and/or hormone receptors on their surface |
| "IQR" | interquartile range, a measure of statisical dispersion, which is the spread of the data |
| "irAE(s)" | immune-related adverse event(s) |
| "mTNBC" | metastatic TNBC |
| "NE" | not evaluable |
| "NSCLC" | non-small cell lung cancer |
| "ORR" | objective response rate |

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| "OS" | overall survival |
| "PD-L1" | programmed death ligand 1, a protein on the surface of a normal cell or a cancer cell that can attach to programmed cell death protein 1 on the surface of the T-cell that causes the T-cell to turn off its ability to kill the cancer cell |
| "PFS" | progression-free survival |
| "Q2W" | once every two weeks |
| "Q3W" | once every three weeks |
| "Q8W" | once every eight weeks |
| "RECIST v1.1" | Response Evaluation Criteria in Solid Tumors, a standard way to measure the response of a tumor to treatment |
| "SABCS 2022" | the 45th San Antonio Breast Cancer Symposium, an international forum for interaction, communication, and education for a broad spectrum of researchers, health professionals, and those with a special interest in BC |
| "SAE(s)" | serious adverse events |
| "TNBC" | triple-negative breast cancer, any breast cancer that does not express the genes for estrogen receptor (ER), progesterone receptor (PR) and HER2/neu |
| "tpCR" | total pathologic complete response |
| "TRAE(s)" | treatment-related adverse event(s) |

**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, or ultimately market, KN046 and KN026, 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, December 9, 2022

*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. XU Zhan Kevin as non-executive Director, and Dr. GUO Zijian, Mr. WEI Kevin Cheng and Mr. WU Dong as independent non-executive Directors.*