ALPHAMAB ONCOLOGY
康寧傑瑞生物製藥
(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 9966)

VOLUNTARY ANNOUNCEMENT

RESEARCH RESULTS ON KN046 AND KN026 PRESENTED AT ESMO CONGRESS 2023

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.

Reference is made to the Company's voluntary announcement dated August 10, 2023. The board of directors of the Company (the "**Board**") is pleased to announce that the research results on KN046 (an anti-PD-L1/CTLA-4 bispecific antibody) and KN026 (a HER2-targeted bispecific antibody) have been presented at the 2023 congress of European Society for Medical Oncology ("**ESMO Congress 2023**"), an influential oncology platform designed in Europe for clinicians, researchers, patient advocates, journalists and healthcare industry representatives from all over the world. Such research results of KN046 and KN026 will also be presented at the Company's website at http://www.alphamabonc.com correspondingly, the summaries of which are set out below:

PRELIMINARY DATA FROM A SINGLE-ARM, OPEN-LABEL, MULTICENTER PHASE II CLINICAL TRIAL: KN046 COMBINED WITH AXITINIB AS FIRST-LINE TREATMENT FOR NSCLC

This is a multicenter and open-label phase II clinical trial designed to evaluate the the efficacy, safety and tolerability of KN046 combined with Axitinib as the first-line treatment for NSCLC. Patients with recurrent or metastatic NSCLC, systemic treatment-naïve and PD-L1 positive (TPS≥1%) were enrolled. This study adopted the Simon's Optimal Two-stage Design: (i) in the first stage, 17 subjects were enrolled, and (ii) in the second stage, enrollment would be discontinued if the objective response (CR or PR) observed is less than 6 subjects; otherwise, 37 subjects will be enrolled in the second stage. The primary endpoint was ORR, and the secondary endpoints included DoR, safety, PFS and OS. Enrolled patients were given KN046 at 5mg/kg Q3W intravenously and Axitinib 5mg two times a day orally.

As of August 8, 2023, 38 subjects were enrolled. Among them, 10 patients (26.3%) had 50% or greater PD-L1 expression, 33 patients (86.8%) were at stage IVa or IVb and 36 patients (94.7%) had an ECOG PS of 1.

- *Efficacy:* Among 29 evaluable patients, the ORR was 58.6% (95% CI: 38.94 to 76.48). Patients with higher PD-L1 expression had a higher ORR. The ORR of patients with 50% or greater PD-L1 expression was 83.3% (95% CI: 35.88 to 99.58). The mPFS follow-up was 4.17 months (95% CI: 1.41 to 6.87), the mPFS was 8.35 months (95% Cl: 5.45 to NE) and the mPFS for non-squamous NSCLC was 9.20 months (95% Cl: 5.59 to NE). The mOS was NR.

- *Safety:* Among all 38 enrolled patients, the incidence rate of KN046-related TRAEs at grade 3 or higher levels according to CTCAE was 23.7% (9 of 38). The most frequent TRAEs included AST increased (7.9%), ALT increased (5.3%), diarrhoea (5.3%) and others（less than 3%）. The irAEs occurred in 6 patients (15.8%), among whom 2 patients (5.3%) experienced irAEs at grade 3 or higher levels according to CTCAE. There was no KN046-related death.

Conclusions: KN046 combined with Axitinib was well tolerated and demonstrated very promising efficacy and safety signal in the first-line treatment for advanced NSCLC. The second stage of enrollment is ongoing and a phase III randomized clinical trial for the first-line NSCLC patient is planned to confirm the combination of KN046 and axitinib as a viable chemo free option.

EFFICACY AND SAFETY OF KN046 IN PATIENTS WITH METASTATIC NSCLC WHO PREVIOUSLY TREATED WITH ICI(s)

The previous phase I ("**KN046-CHN-001**") and phase II ("**KN046-201**") clinical trials designed to assess the efficacy, safety and tolerability of KN046 in NSCLC showed promising antitumor efficacy of KN046 in NSCLC patients who had failed prior ICI(s) therapy. The further efficacy and safety results of KN046 in NSCLC patients who had failed prior ICI(s) therapy from KN046-CHN-001 and the cohort C of KN046-201 are presented below.

From April 19, 2019 to July 13, 2020, 31 patients with metastatic NSCLC that progressed after ICI(s) and platinum-based chemotherapy were enrolled, but patients with EGFR mutation and/or ALK translocation were excluded. All patients were given KN046 (26 patients at 5mg/kg Q2W, 2 patients at 5mg/kg Q3W, 2 patients at 300mg Q3W and 1 patient at 3mg/kg Q2W) intravenously. The primary endpoints were confirmed ORR according to RECIST v1.1 and safety.

As of July 30, 2022 for KN046-201 and August 31, 2021 for KN046-CHN-001, the median follow-up was 25.0 months (95% CI: 24.4 to NE).

- *Efficacy:* Among all 31 patients, the ORR was 3.2% (95% CI: 0.1 to 16.7), the DCR was 38.7% (95% CI: 21.8 to 57.8), the CBR was 16.1% (95% CI: 5.5 to 33.7). The mPFS was 2.8 months (95% CI: 1.8 to 3.7), mOS was 13.3 months (95% CI: 6.5 to 17.5) and the 12-month OS rate was 54.8% (95% CI: 35.97 to 70.26).

- *Safety:* TRAEs at grade 3 or higher levels occurred in 7 patients (22.6%). Commonly reported TRAEs at grade 3 or higher levels were anemia (9.7%), febrile neutropenia (3.2%) and fatigue (3.2%), etc.

Conclusions: KN046 was well tolerated and demonstrated encouraging results especially in OS benefit in NSCLC patients who had failed prior ICI(s) therapy.

UPDATED RESULTS OF THE EFFICACY AND SAFETY OF KN046 IN PATIENTS WITH METASTATIC NSCLC WHO FAILED PRIOR EGFR-TKI(s)

This is an open-label, multicenter, single-arm clinical trial designed to evaluate the efficacy, safety and tolerability of KN046 combined with chemotherapy for the treatment of NSCLC. This clinical trial enrolled patients with EGFR sensitivity mutation who had failed prior EGFR-TKIs without platinum-based chemotherapy.

From January 7, 2020 to December 17, 2021, 26 patients with metastatic NSCLC were enrolled. They were given KN046 at 5mg/kg Q3W in combination with chemotherapy (Pemetrexed, at 500mg/m^2 Q3W and Carboplatin at AUC=5 Q3W) until the occurrence of disease progression, intolerable toxicity and other discontinuation criteria. The primary endpoint was confirmed ORR according to RECIST v1.1.

KN046 combined with chemotherapy had demonstrated the efficacy and safety in advanced NSCLC with EGFR sensitivity mutation who progressed after TKI(s), the details of which are set out in the Company's voluntary announcement dated September 5, 2022, followed by which an updated analysis in relation to its survival and safety data are presented below:

As of July 30, 2022, the median follow-up was 17.8 months (95% CI: 13.0 to 19.5).

- *Efficacy:* Among all 26 patients, the ORR was 26.9% (95% CI: 11.6 to 47.8) with 5 patients (19.2%) of tumor shrinkage rate of 50% or higher, the DCR was 84.6% (95% CI: 65.1 to 95.6) with 7 PR and 15 SD, and the CBR was 38.5% (95% CI: 20.2 to 59.4). The mPFS was 5.5 months (95% CI: 4.2 to 6.8), the mOS was 20.2 months (95% CI: 11.5 to NR) and the 12-month OS rate was 65.29% (95% CI: 42.16 to 81.02).

- *Safety:* TRAEs at grade 3 or higher levels occurred in 15 patients (57.7%). The most common (10% or more) TRAEs were anemia (42.3%), AST increased (42.3%), ALT increased (34.6%) and infusion-related reaction (30.8%), etc.

Conclusions: KN046 demonstrated encouraging efficacy results especially in OS benefit and a favorable safety profile in advanced NSCLC patients with EGFR sensitivity mutation who progressed after EGFR-TKI(s).

KN046 IN PATIENTS WITH ≥2L RECURRENT/METASTATIC THYMIC CARCINOMA: A PROSPECTIVE, SINGLE-ARM, MULTICENTER, PHASE II STUDY

This is a phase II clinical trial designed to evaluate the efficacy and safety of KN046 in patients with refractory or metastatic thymic carcinoma who progressed after front-line chemotherapy. The primary endpoint was ORR evaluated by the independent review committee, and the secondary endpoints were PFS, OS, DOR, safety and tolerability.

Patients with metastatic or inoperable locally advanced thymic carcinoma who progressed after at least one platinum-containing chemotherapy were enrolled. KN046 was given at 5mg/kg Q2W intravenously until the occurrence of disease progression or unacceptable toxicity or the withdrawal of consent.

From December 2020 to December 2022, 48 patients were enrolled, among whom 46 patients (96%) were at stage IVb. There were 17 patients (35.0%) with PD-L1 positive (TPS≥1%), 25 patients (52.0%) with PD-L1 negative (TPS＜1%) and 6 patients (13.0%) whose status were unknown.

As of August 30, 2023, the median follow-up was 21.5 months (interquartile range: 16.7 to 24.8 months).

- *Efficacy:* Among 45 evaluable patients, 6 patients (13.3%) achieved PR and 20 patients (44.4%) remained SD. The ORR was 15.6% (95% CI: 6.5 to 29.5), the DCR was 60.0% (95% CI: 44.3 to 74.3) and the DoR was 14.7 months (95% CI: 1.9 to NE). The mPFS was 3.9 months (95% CI: 1.3 to 11.3). Among the patients with PD-L1 positive (TPS ≥1%), the mPFS was 5.7 months (95% CI: 1.8 to NE). The median OS was immature with the 12-month OS rate of 92.4% (95% CI: 78.3 to 93.5) and the 24-month OS rate of 72.1% (95% CI: 53.8 to 84.4), respectively, which were numerically higher than the historical clinical data reported in the literature.

- *Safety:* All 48 patients tolerated well to KN046, among whom the SAEs occurred in 19 patients (39.6%) with no TEAE leading to death. The most common (20% or more) TRAEs at all grades included rash (37.5%), AST increased (31.3%), ALT increased (27.1%), anemia (22.9%), and fatigue (22.9%).

Conclusions: KN046 demonstrated promising antitumor activity and acceptable toxicity in thymic carcinoma patients who had received at least one line of chemotherapy. As of the date of data cut-off, the mOS was not mature and there was still more than half of patients alive, demonstrating an encouraging signal in survival benefit.

TWO-YEAR FOLLOW-UP DATA ON THE EFFICACY AND SAFETY OF KN026 COMBINED WITH DOCETAXEL AS FIRST-LINE TREATMENT FOR HER2-POSITIVE RECURRENT OR METASTATIC BC

The preliminary safety and efficacy results of KN026 combined with Docetaxel as the first-line treatment for HER2-positive recurrent or metastatic BC were presented at the San Antonio Breast Cancer Symposium in 2022, showing promising efficacy and tolerability. The 2-year follow-up results are updated below.

This clinical trial enrolled eligible patients with recurrent or metastatic BC, HER-2 positive and treatment-naïve. Patients were given KN026 30mg/kg combined with Docetaxel 75mg/m^2 Q3W until the occurance of disease progression, unacceptable toxicity, or other reasons. The primary endpoints were ORR and DoR. The secondary endpoints included safety, PFS and OS.

As of August 4, 2023, 57 patients were enrolled with the median age of 52 years old (aged from 30 to 67). All patients were female, among whom 52 patients (91.2 %) were at stage IV. The most common sites of metastasis were lymph nodes, bone, lung and liver.

- *Efficacy:* The confirmed ORR of 55 evaluable patients was 76.4% (95% CI: 62.98 to 86.77) and DCR was 100% (95% CI: 93.51 to 100). The median DoR follow-up was 26.3 months (95% CI: 23.92 to 28.91) and the DoR was 26.8 months (95% CI: 20.73 to NE). The median study follow-up was 29.7 months (95% CI: 28.32 to 30.59), the mPFS was 26.9 months (95% Cl: 17.97 to NE) and the mOS was NR. But the 12-month, 24-month and 30-month OS rates were 93.0% (95% Cl: 82.37 to 97.31), 84.2% (95% Cl: 71.85 to 91.45) and 77.9% (95% Cl: 64.17 to 86.89), respectively.

- *Safety:* TEAEs at grade 3 or higher levels occurred in 35 patients (61.4%) and there was no death due to KN026-related adverse events. The incidence rate of KN026-related TRAEs at grade 3 or higher levels was 40.4% (23 of 57), including neutrophil count decreased (24.6%), white blood cell count decreased (12.3%) and others (less than 10%).

Conclusions: KN026 in combination with Docetaxel was well tolerated and had shown promising clinical benefit as first-line treatment for HER2-positive BC. After 2 years of follow-up, the mPFS was 26.9 months and the 24-month OS rate was 84.2%, which is promising. Robustness of efficacy and safety results will be further confirmed in an ongoing randomized phase III clinical trial with trastuzumab plus pertuzumab and Docetaxel as control.

KN026 IN COMBINATION WITH DOCETAXEL AS NEOADJUVANT TREATMENT FOR HER2+ EARLY OR LOCALLY ADVANCED BC: A SINGLE ARM, MULTICENTER, PHASE II STUDY

This is a single-arm, multicenter phase II clinical trial designed to evaluate the efficacy and safety of KN026 in combination with Docetaxel as neoadjuvant treatment for HER2+ early or locally advanced BC. The primary endpoint was tpCR rate and the secondary endpoints were bpCR, ORR, safety, pharmacokinetics and immunogenicity.

From August 9, 2021 to July 29, 2022, 30 patients were enrolled: (i) 16 patients (53.3%) were at stage II, (ii) 14 patients (46.7%) were at stage III, (iii) 26 patients (86.7%) were with biopsy-confirmed lymph node metastases, (iv) all were HER2-positive and (v) 15 patients (50.0%) were hormone receptor positive. They received 4 cycles of KN026 (30mg/kg, ivgtt d1, Q3W) and Docetaxel (75mg/m^2, ivgtt d1, Q3W) as neoadjuvant treatment.

As of November 21, 2022, 28 patients (93.3%) completed the surgery followed by pathological evaluation.

- *Efficacy:* Among all 30 patients, the tpCR rate was 56.7% (95% CI: 37.43 to 74.54), the posterior probability for tpCR more than 40% was 96.7%, the bpCR rate was 60.0% (95% CI: 40.60 to 77.34), the confirmed ORR was 86.7% (95% CI: 69.28 to 96.24).

- *Safety:* Among all 30 patients, 16 patients (53.3%) experienced the TEAEs at grade 3 or higher levels according to CTCAE. The most common (5% or more) TEAEs at grade 3 or higher levels were neutrophil count decreased (50.0%), white blood cell count decreased (40.0%), and lymphocyte count decreased (10.0%). SAEs at grade 3 or higher levels occurred in 2 patients (6.7%). SAE related to KN026 occurred in only one patient (3.33%).

Conclusions: KN026 combined with Docetaxel as neoadjuvant treatment demonstrated 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, triple-negative BC, 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 triple-negative BC 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 ICIs. The Group is conducting pivotal clinical trials in NSCLC and pancreatic ductal adenocarcinoma. 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 BC and gastric cancer/gastroesophageal junction cancer. Currently, two phase III clinical trials of KN026 as second-line or above treatment of HER2-positive gastric cancer/gastroesophageal junction cancer and as first-line treatment of HER2-positive BC are 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 National Medical Products Administration of China (國家藥品監督管理局), 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.

"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
"ALK"	anaplastic lymphoma kinase
"ALT"	alanine transaminase
"AST"	aspartate transaminase
"AUC"	area under the free carboplatin plasma concentration versus time curve, used as Carboplatin dosage value
"Axitinib"	a targeted cancer drug used to treat kidney cancer after previous treatment has not been effective
"BC"	breast cancer
"bpCR"	breast pathologic complete response
"Carboplatin"	a chemotherapy treatment for many different types of cancer
"CBR"	clinical benefit rate
"China"	the People's Republic of China, except where the context requires otherwise, excluding Hong Kong, the Macau Special Administrative Region of the People's Republic of China and Taiwan
"CR"	complete response
"CTCAE"	Common Terminology Criteria for Adverse Events, which is widely accepted as the standard classification and severity grading scale for adverse events in cancer therapy, clinical trials and other oncology settings
"CTLA-4"	cytotoxic T-lymphocyte-associated protein 4
"d1"	the first day of treatment
"DCR"	disease control rate
"Director(s)"	the directors of our Company, including all executive, non-executive and independent non-executive directors
"Docetaxel"	a chemotherapy medication used to treat a number of types of cancer
"DoR"	duration of response

"ECOG PS"	ECOG Scale of Performance Status, one standard criteria describing a patient's level of functioning in terms of their ability to care for themself, daily activity and physical ability (walking, working, etc.). ECOG PS 0 means the patient is fully active, able to carry on all pre-disease performance without restriction. ECOG PS 1 means the patient is restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
"EGFR"	epidermal growth factor receptor
"EGFR-TKI(s)"	epidermal growth factor receptor tyrosine kinase inhibitor(s), used in the first-line treatment of NSCLC
"HER2"	human epidermal growth factor receptor 2
"HER2-positive"	HER2 IHC 3+ or HER2 gene amplification
"ICI(s)"	immune checkpoint inhibitor(s), molecules that release the natural brakes of immune response
"IHC"	Immunohistochemistry, which tests whether or not the cancer cells have HER2 receptors and/or hormone receptors on their surface
"irAE(s)"	immune-related adverse event(s)
"ivgtt"	intravenous infusion
"mOS"	median overall survival
"mPFS"	median PFS
"NE"	not evaluable
"NR"	not reached
"NSCLC"	non-small cell lung cancer
"ORR"	objective response rate
"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 PD-1 on the surface of the T-cell that causes the T-cell to turn off its ability to kill the cancer cell
"Pemetrexed"	an antineoplastic agent approved for the treatment of non-squamous NSCLC and mesothelioma
"PFS"	progression-free survival, the length of time during and after the treatment that a patient lives without the disease getting worse

"PR"	partial response
"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
"SD"	stable disease
"Simon's Optimal Two-stage Design"	a type of phase II clinical trial which allows flexibility regarding the null and alternative hypotheses while also allowing stopping for futility
"TEAE(s)"	treatment emergent adverse event(s)
"tpCR"	total pathologic complete response
"TPS"	tumor proportion score
"TRAE(s)"	treatment-related adverse event(s)
"SAE(s)"	serious adverse event(s)
"%"	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, 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, October 23, 2023

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