CARsgen Therapeutics Holdings Limited
科濟藥業控股有限公司
(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 2171)

VOLUNTARY ANNOUNCEMENT UPDATED RESEARCH RESULTS ON CT041 AT 2024 ASCO GI MEETING

This announcement is made by CARsgen Therapeutics Holdings Limited (the "**Company**", together with its subsidiaries and consolidated affiliated entities, the "**Group**" or "**CARsgen**") on a voluntary basis to inform the shareholders and potential investors of the Company about the latest business update of the Group.

The board of directors of the Company (the "**Board**") announces that at the 2024 American Society of Clinical Oncology Gastrointestinal Cancers Symposium ("**ASCO GI**"), the Company presented a poster with study results for satricabtagene autoleucel ("**satri-cel**", R&D code: CT041, an autologous CAR-T product candidate against Claudin18.2), which include the dose escalation results of the Phase 1b ELIMYN18.2 study (Cohort A) in gastric/gastroesophageal (GC/GEJ) or pancreatic cancer (PC) in the US. Details are listed below:

Poster #356: CLDN18.2 Chimeric Antigen Receptor T Cell Therapy for Patients with Advanced Gastric and Pancreatic Adenocarcinoma: Results of ELIMYN18.2 Phase 1b Clinical Trial

The single-arm, open-label, Phase 1b/2 study (NCT04404595) evaluated the safety and efficacy of satri-cel in patients with Claudin18.2-positive histologically confirmed advanced GC/GEJ or PC who had progressed or were intolerant of at least 2 prior lines (GC/GEJ) or 1 prior line (PC) of systemic therapy. The Phase 1b study consisted of a modified 3+3 dose escalation/de-escalation with 5 dose levels (DLs) to be tested. Patients received a preconditioning regimen of fludarabine, cyclophosphamide, and nab-paclitaxel, followed by 1-3 cycles of satri-cel.

Herein, the Company presented the updated results of safety and determination of the Recommended Phase 2 Dose (RP2D). DL3 (600×10^6 cells) was selected as RP2D and enrollment in Phase 2 is currently ongoing. Adverse Events (AEs) were graded per CTCAE Version 5.0 and CRS and ICANS were graded by ASTCT 2019 consensus criteria. Objective Response Rate (ORR) and Clinical Benefit Rate (CBR) were assessed per RECIST 1.1, and tumor response (CR or PR) was confirmed by an imaging scan after the initial response assessment. CBR is defined as the incidence of a best overall response of CR, PR, or SD≥180 days.

As of September 15, 2023, the median follow-up duration was 8.9 months (range:1.5-18.7 months). 19 patients were treated (7 GC/GEJ, 12 PC) across 3 DLs ranging from 250-600×10^6 cells: DL1: 250-300×10^6 (n=6), DL2: 375-400×10^6 (n=6), DL3: 600×10^6 (n=7). All patients received prior systemic therapy, among which 6 GC/GEJ (85.7%) and 7 PC (58.3%) patients received ≥ 3 lines of prior systemic treatment. Median number of prior systemic treatment lines of patients with GC/GEJ or PC were 4 (2,10) and 3 (1,5) respectively. Median number of metastatic organs of all patients was 2.0. All patients received at least one infusion and median number of infusions for all patients was 2.0 (1,3).

Safety

Overall, the safety profile of satri-cel was encouraging. No hemophagocytic lymphohistiocytosis (HLH), dose-limiting toxicities (DLTs), or treatment-related deaths were reported. The vast majority of CRS was Grade 1 with three Grade 2 events and two Grade 3 events. Apart from 1 patient who experienced Grade 1 immune effector cell-associated neurotoxicity syndrome (ICANS), no other ICANS events of any grade were observed. All events resolved.

Efficacy

As of September 15, 2023, the median follow-up duration was 8.9 months (range:1.5 to 18.7 months). 1 patient with GC/GEJ in DL3 achieved a CR. The confirmed ORR in patients with GC/GEJ in all DLs was 42.9% (3/7). CBR in patients with GC/GEJ or PC in DL3 was 71.4% (5/7) and in patients with GC/GEJ in all DLs was 57.1% (4/7). The median progression-free survival (mPFS) and median duration of response (mDOR) was 5.7 months and 6.9 months respectively in patients with GC/GEJ in all DLs. In DL3, median overall survival (mOS) in patients with GC/GEJ or PC was 12.9 months. The mOS in patients with GC/GEJ or PC in all DLs was 8.9 months.

Conclusion

The safety profile of satri-cel, the first autologous Claudin18.2 CAR T cell therapy, was encouraging. Initial efficacy was promising in heavily pre-treated Claudin18.2-positive advanced GC/GEJ and PC population and consistent with earlier reports.

ABOUT SATRI-CEL

Satri-cel (CT041) is an autologous CAR T-cell product candidate against the protein Claudin18.2 that has the potential to be the first-in-class globally. Satri-cel targets the treatment of Claudin18.2 positive solid tumors with a primary focus on gastric cancer/gastroesophageal junction cancer (GC/GEJ) and pancreatic cancer (PC). Trials in CARsgen include investigator-initiated trials (NCT03874897), a Phase Ib clinical trial for advanced GC/GEJ and PC and a confirmatory Phase II clinical trial for advanced GC/GEJ in China (CT041-ST-01, NCT04581473), a Phase I clinical trial for PC adjuvant therapy in China (CT041-ST-05, NCT05911217), and a Phase 1b/2 clinical trial for advanced gastric or pancreatic adenocarcinoma in North America (CT041-ST-02, NCT04404595). Satri-cel was granted Regenerative Medicine Advanced Therapy (RMAT) Designation by U.S. FDA for the treatment of advanced GC/GEJ with Claudin18.2-positive tumors in January 2022 and was granted PRIME eligibility by the EMA for the treatment of advanced gastric cancer in November 2021. Satri-cel received Orphan Drug designation from the U.S. FDA in 2020 for the treatment of GC/GEJ and Orphan Medicinal Product designation from the EMA in 2021 for the treatment of advanced gastric cancer.

ABOUT THE COMPANY

CARsgen is a biopharmaceutical company with operations in China and the U.S. and is focused on innovative CAR T-cell therapies for the treatment of hematologic malignancies and solid tumors. CARsgen has established a comprehensive CAR T-cell research and development platform, encompassing target discovery, innovative CAR T-cell development, clinical trials, and commercial-scale production. CARsgen has internally developed novel technologies and a product pipeline with global rights to address major challenges of CAR T-cell therapies, such as improving the safety profile, enhancing the efficacy in treating solid tumors, and reducing treatment costs. CARsgen's vision is to become a global biopharmaceutical leader that brings innovative and differentiated cell therapies to cancer patients worldwide and makes cancer curable.

DEFINITIONS AND GLOSSARY OF TECHNICAL TERMS

"ASTCT"	American Society for Transplantation and Cellular Therapy
"CAR"	chimeric antigen receptor
"CAR T"	chimeric antigen receptor T cell
"CLDN18.2" or "Claudin18.2"	a protein found on the cells of certain solid tumors such as gastric cancer and pancreatic cancer, which makes the protein an attractive target for treatment
"confirmatory trial" or "pivotal trial"	the controlled trial or study intended to demonstrate the required clinical efficacy and safety evidence before submission for drug marketing approval
"CTCAE"	Common Terminology Criteria for Adverse Events
"EMA"	European Medicines Agency
"FDA" or "U.S. FDA"	U.S. Food and Drug Administration
"Investigator-initiated trial"	clinical trial sponsored and conducted by independent investigators
"Phase Ib"	a phase of clinical trials that primarily assesses safety, tolerability and pharmacokinetics/pharmacodynamics at multiple ascending dose levels prior to commencement of a Phase II or Phase III clinical trial
"Phase II clinical trial"	a study in which a drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug for a specific targeted disease, and to determine dosage tolerance and optimal dosage

"PRIME"	PRIority MEdicine. A scheme launched by the EMA to offer early and proactive support to medicine developers to optimize the generation of robust data on a medicine's benefits and risks, and to accelerate the assessment of the applications of medicines that target an unmet medical need with advantages over existing treatments
"RECIST"	Response Evaluation Criteria in Solid Tumors
"regenerative medicine advanced therapy" or "RMAT"	a special status granted by the FDA to regenerative medicine therapies, including cell therapies, that are intended to treat a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition
"solid tumor"	an abnormal mass of tissue that usually does not contain cysts or liquid areas
"United States" or "U.S."	the United States of America, its territories, its dependencies and all areas subject to its jurisdiction

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, satri-cel successfully. Shareholders and potential investors of the Company are advised to exercise caution when dealing in the shares of the Company.

Cautionary-Language Regarding Forward-Looking Statements

All statements in this announcement that are not historical fact or that do not relate to present facts or current conditions are forward-looking statements. Such forward-looking statements express the Group's current views, projections, beliefs and expectations with respect to future events as of the date of this announcement. Such forward-looking statements are based on a number of assumptions and factors beyond the Group's control. As a result, they are subject to significant risks and uncertainties, and actual events or results may differ materially from these forward-looking statements and the forward-looking events discussed in this announcement might not occur. Such risks and uncertainties include, but are not limited to, those detailed under the heading "Principal Risks and Uncertainties" in our most recent annual report and interim report and other announcements and reports made available on our corporate website, https://www.carsgen.com. No representation or warranty is given as to the achievement or reasonableness of, and no reliance should be placed on, any projections, targets, estimates or forecasts contained in this announcement.

By order of the Board
CARsgen Therapeutics Holdings Limited
Dr. Zonghai LI
Chairman

Hong Kong, January 19, 2024

As at the date of this announcement, the board of directors of the Company comprises Dr. Zonghai LI, Dr. Huamao WANG and Dr. Hua JIANG as executive Directors; Mr. Bingsen GUO, Mr. Huaqing GUO and Mr. Ronggang XIE as non-executive Directors; Dr. Guangmei YAN, Dr. Huabing LI and Ms. Xiangke ZHAO as the independent non-executive Directors.

In the case of inconsistency, the English text of this announcement shall prevail over the Chinese text.