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 ZEVORCABTAGENE AUTOLEUCEL PRESENTED AT 2022 ASH ANNUAL 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 2022 American Society of Hematology (the "**ASH**") Annual Meeting, the Company presented a poster with the results of the phase II LUMMICAR STUDY 1 clinical trial of zevorcabtagene autoleucel ("**zevor-cel**", R&D code: CT053, an autologous CAR T-cell product candidate against BCMA) in Chinese patients with relapsed/refractory multiple myeloma (R/R MM). This poster reports for the first time the pivotal phase II safety and efficacy data of LUMMICAR STUDY 1.

Poster: Phase II Study of Fully Human BCMA-Targeted CAR T Cells (Zevorcabtagene Autoleucel) in Patients with Relapsed/Refractory Multiple Myeloma

Zevor-cel, a fully human autologous CAR T-cell product targeting B-cell maturation antigen (BCMA), is being evaluated for patients with R/R MM in LUMMICAR STUDY 1 (NCT03975907), an ongoing phase I/II clinical trial in China. Results for the 14 subjects treated in phase I of LUMMICAR STUDY 1 showed a well-tolerated safety profile, plus deep and durable responses with an objective response rate (ORR) of 100% and a complete response/stringent complete response (CR/sCR) rate of 78.6%.

A total of 102 patients with R/R MM were treated with zevor-cel at the dose of 150×10^6 CAR+ T cells. The patients had a median age of 59.5 years, the median time from diagnosis was 3.6 years, and the median prior lines of therapy was 4 (range, 3-15). Of the treated patients, 39 (38.2%) had International Staging System stage III disease; 46 (45.1%) patients had high-risk cytogenetic abnormalities, defined as del (17p), t (4;14), t (14;16), t (14;20); and 24 (23.5%) patients had received autologous stem cell transplantation. The lymphodepletion regimen comprised cyclophosphamide at 300 mg/m^2 and fludarabine at 25 mg/m^2 daily for 3 days before zevor-cel treatment.

Safety

Zevor-cel was well tolerated with manageable safety profile. The treatment-related adverse events (AEs) were reported for 102 patients, and the AEs mainly comprised the lymphodepletion-related hematologic toxicities. A total of 92 (90.2%) patients experienced cytokine release syndrome (CRS) with 7 (6.9%) at grade 3 or 4, and all patients recovered from CRS. No grade 3 or higher neurotoxicity was identified. Two immune effector cell-associated neurotoxicity syndrome (ICANS) events (both grade 1) occurred, and the patients recovered without the use of tocilizumab or steroids. Treatment-related serious adverse events (SAEs) occurred in 38 (37.3%) patients, mainly comprising hematologic toxicities and infections. No AE led to discontinuation of zevor-cel infusion. One treatment-related death occurred 5 months post CAR T-cell infusion from severe pneumonia in a patient who had a history of chronic pneumonia.

Efficacy

At the update cut-off date of August 16, 2022, 102 patients had at least 3 months follow-up or early withdrawal, among whom 60 patients had at least 6 months follow-up or early withdrawal. For all 102 patients, the median follow-up was 9 months (range, 0.4-17.8 months), the ORR was 92.2% (95% CI, 85.13, 96.55), the rate of very good partial response (VGPR) or better was 85.3%, and the CR/sCR rate was 45.1%. Further, among the first 60 patients treated in the current study with a median follow-up of 12.1 months (0.4-17.8 months), the CR/sCR rate was 56.7%. The median DOR and median PFS were not reached. At 9 months median follow-up, the DOR rate was 86.1% and the PFS rate was 84.6%. Minimal residual disease (MRD) status was assessed in patients achieving VGPR or better. The MRD negativity rate (sensitivity of $<10^{-5}$ nucleated cells) was 100% in patients with CR/sCR and 96.3% in patients with VGPR or better.

Conclusion

Preliminary results of the pivotal phase II LUMMICAR STUDY 1 showed that zevor-cel delivered deep and durable responses in patients with heavily pre-treated R/R MM.

ABOUT ZEVOR-CEL

Zevor-cel (CT053) is a fully human, autologous BCMA CAR T-cell product candidate for the treatment of R/R MM. The New Drug Application (NDA) for zevor-cel based on the phase I/II data from LUMMICAR STUDY 1 in China has been accepted by NMPA. CARsgen is conducting the phase 1b/2 LUMMICAR STUDY 2 clinical trial in North America to evaluate the safety and efficacy of zevor-cel for R/R MM in that population. The Company also plans to conduct additional clinical trials to develop zevor-cel as an earlier line of treatment for multiple myeloma.

Zevor-cel received Regenerative Medicine Advanced Therapy (RMAT) and Orphan Drug designations from the U.S. FDA in 2019, as well as the Priority Medicines (PRIME) and Orphan Medicinal Product designations from the European Medicines Agency (EMA) in 2019 and 2020, respectively. Zevor-cel also received Breakthrough Therapy designation from the NMPA in 2020.

The Company believes that zevor-cel is well positioned to potentially reshape the treatment paradigm for multiple myeloma and become a foundational treatment for multiple myeloma patients.

ABOUT THE COMPANY

CARsgen is a biopharmaceutical company with operations in China and the U.S. mainly focused on innovative CAR T-cell therapies for the treatment of hematologic malignancies and solid tumours. The Company has built an integrated cell therapy platform with in-house capabilities that span target discovery, lead antibody development, clinical trials, and commercial-scale manufacturing. 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 tumours, and reducing treatment costs. Our 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

"AE"	Adverse event, AEs were collected from the time of informed consent
"BCMA"	B-cell maturation antigen, a protein that is highly expressed in several hematologic malignancies
"CAR"	Chimeric antigen receptor
"CAR T"	Chimeric antigen receptor T cell
"CI"	Confidence interval
"CR"	Complete response
"CRS"	Cytokine release syndrome, a form of systemic inflammatory response syndrome that arises as a complication of some diseases or infections, and is also an adverse effect of some monoclonal antibody drugs, as well as adoptive T cell therapies
"DOR"	Duration of objective response
"EMA"	European Medicines Agency
"FDA" or "U.S. FDA"	Food and Drug Administration
"ICANS"	Immune effector cell-associated neurotoxicity syndrome, a potentially life-threatening neurotoxicity that commonly occurs with CAR T-cell therapy
"IRC"	Independent review committee
"MM"	Multiple myeloma

"MRD"	Minimal residual disease, a sensitivity marker for prognostic indicator
"NMPA"	National Medical Products Administration (國家藥品監督管理局), the successor of the China Food and Drug Administration (國家食品藥品監督管理總局), or the CFDA, the State Food and Drug Administration (國家食品藥品監督管理局), or the SFDA and the State Drug Administration (國家藥品監督管理局), or the SDA
"ORR"	Objective response rate
"PFS"	Progression-free survival
"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 trials
"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 specific targeted disease, and to determine dosage tolerance and optimal dosage
"Pivotal trial"	The final trial or study to demonstrate clinical efficacy and safety evidence required before submission for drug marketing approval
"PR"	Partial response
"RMAT"	Regenerative medicine advanced therapy, a special status granted by the FDA to regenerative medicine therapies, including cell therapies, intended to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition
"R/R"	Relapsed/refractory
"SAE"	Serious adverse event
"sCR"	Stringent complete response
"U.S."	The United States of America, its territories, its dependencies, and all areas subject to its jurisdiction
"VGPR"	Very good partial response
"zevor-cel"	Zevorcabtagene autoleucel

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, zevorcabtagene autoleucel successfully. Shareholders and potential investors of the Company are advised to exercise caution when dealing in the shares of the Company.

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

Hong Kong, December 12, 2022

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. Chunhai FAN, Dr. Guangmei YAN and Mr. Tak Young SO as the independent non-executive Directors.

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