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)

ANNOUNCEMENT OF ANNUAL RESULTS FOR THE YEAR ENDED DECEMBER 31, 2021

The board (the "**Board**") of directors (the "**Directors**") of CARsgen Therapeutics Holdings Limited (the "**Company**", "**CARsgen Therapeutics**" or "**CARsgen**") is pleased to announce the audited consolidated results of the Company, its subsidiaries and consolidated affiliated entities (collectively, the "**Group**") for the year ended December 31, 2021 (the "**Reporting Period**"), together with the audited comparative figures for the year ended December 31, 2020.

FINANCIAL HIGHLIGHTS

	Year ended December 31	
	2021	2020
	RMB'000	*RMB'000*
Net loss	**(4,744,423)**	(1,064,049)
Net loss per share	**(12.26)**	(5.37)
Non-IFRS Measures		
Adjusted net loss[(1)]	**(548,767)**	(333,725)
Adjusted net loss per share[(1)]	**(1.42)**	(1.68)

	As at December 31	
	2021	2020
	RMB'000	*RMB'000*
Cash and cash equivalents	**691,284**	1,042,969
Terms deposits with original maturity between three and twelve months	**2,315,654**	–
Total	**3,006,938**	1,042,969

Our net loss was RMB4,744 million for the year ended December 31, 2021, representing an increase of RMB3,680 million from RMB1,064 million for the year ended December 31, 2020. The increase was primarily due to (i) the increase of fair value loss in financial instruments issued to investors (the "**Fair Value Loss**"), which totaled RMB4,156 million for the year ended December 31, 2021, representing an increase of RMB3,432 million from RMB724 million for the year ended December 31, 2020. Fair value loss related financial instruments were converted to ordinary shares upon the completion of the Company's initial public offering in June 18, 2021 (the "**IPO**"), hence no loss would be recognized after the IPO; (ii) the listing fees of approximately RMB27 million (the "**Listing Fees**") for the year ended December 31, 2021, representing an increase of RMB23 million from RMB4 million for the year ended December 31, 2020; (iii) the share-based compensation (together with the Fair Value Loss and the Listing Fees, collectively the "**Adjusted Items**"), which totaled RMB14 million for the year ended December 31, 2021, representing an increase of RMB12 million from RMB2 million for the year ended December 31, 2020; and (iv) higher research and development expenses and higher administrative expenses.

Our adjusted net loss*Note (1)* was RMB549 million for the year ended December 31, 2021, representing an increase of RMB215 million from RMB334 million for the year ended December 31, 2020. The increase was primarily due to higher research and development expenses and higher administrative expenses.

Cash and cash equivalents and short-term investments were RMB3,007 million as of December 31, 2021, representing an increase of RMB1,964 million from RMB1,043 million as of December 31, 2020. The increase mostly resulted from proceeds received during the Company's IPO.

Note (1) Adjusted net loss and adjusted net loss per share are non-IFRS measures. They exclude the impact of the Adjusted Items. For details of non-IFRS measures, please refer to "Non-IFRS Measures" subsection for details.

BUSINESS HIGHLIGHTS

On 18 June 2021 (the "**Listing Date**"), the Company was successfully listed on The Stock Exchange of Hong Kong Limited (the "**Stock Exchange**"). During the Reporting Period, we have made significant advancements in the clinical development of our pipeline products, innovation of technology advancement, expansion of manufacturing facilities and establishment of external partnerships. Specifically, we made progress in the following areas:

CT053

CT053 is an autologous CAR T-cell product candidate against BCMA being developed for the treatment of relapsed/refractory multiple myeloma (R/R MM). We have completed patient enrollment in our pivotal Phase II trial in China. In addition, we have started our pivotal Phase 2 clinical trial in North America and treated our first patient in the pivotal Phase 2 trial in August 2021. As communicated with the U.S. FDA, we are adding outpatient administration of CT053 into our U.S. clinical investigations. We plan to submit the NDA to the NMPA in the first half of 2022 and plan to submit the BLA to the U.S. FDA in 2023. We also plan to conduct additional clinical trials to develop CT053 as an earlier line of treatment for multiple myeloma.

Additional data update from the Phase I/II study in China (LUMMICAR STUDY 1) and an integrated analysis in patients with R/R MM by high-risk factors have been available as posters at the 2021 American Society of Hematology ("**ASH**") Annual Meeting in December 2021.

CT041

CT041 is an autologous CAR T-cell product candidate against the protein CLDN18.2 and has the potential to be first-in-class globally. CT041 targets the treatment of CLDN18.2 positive solid tumors with a primary focus on gastric/gastroesophageal junction cancer (GC/GEJ) and pancreatic cancer (PC). We have initiated the investigator-initiated trials, a Phase Ib clinical trial for advanced GC/GEJ and PC and a confirmatory Phase II clinical trial for advanced GC/GEJ in China, and initiated a Phase 1b clinical trial for advanced gastric or pancreatic adenocarcinoma in North America. We plan to submit an NDA to the NMPA in China in the first half of 2024 and also plan to initiate a Phase 2 clinical trial in the second half of 2022 in North America.

Additional data update from a China Investigator-Initiated Trial has been available as an oral presentation at the European Society for Medical Oncology Congress 2021 ("**ESMO Congress 2021**") in September 2021.

CT011

CT011 is a CAR T-cell product candidate with proof-of-concept clinical data for the treatment of hepatocellular carcinoma (HCC) and has the potential to be the first-in class globally. We have completed patients enrollment of a Phase I trial in China.

AB011

AB011 is a humanized monoclonal antibody product candidate against CLDN18.2 being developed for the treatment of CLDN18.2 positive solid tumors. During the second quarter of 2021, we received supplemental application approval by CDE regarding the addition of a chemotherapy combination cohort with AB011 in Phase Ib, and we have subsequently initiated the combination cohort of AB011 with chemotherapy. We completed phase I monotherapy cohort enrollment and initiated combination with chemotherapy. We plan to consult with the NMPA in the second half of 2022 and to initiate the subsequent Phase II clinical trial.

Discovery and Pre-clinical Development

In addition to the existing technologies and clinical pipeline product candidates, which have shown promising efficacy and favorable safety profiles against hematologic malignancies and solid tumors, we continue to dedicate ourselves to advancing innovative CAR T technologies to address major challenges in the industry.

We are focusing on the following major research areas:

(1) Increasing efficacy against solid tumors: developing innovative technologies, such as our CycloCAR® technology, to enhance efficacy of CAR T cells against solid tumors;

(2) Enhancing safety profiles: developing innovative technologies to minimize safety concerns including CRS, neurotoxicity and on-target off-tumor toxicities;

(3) Expanding patient accessibility: advancing our differentiated allogeneic THANK-uCAR® technology to reduce costs and increase affordability. THANK-uCAR® technology has the potential to overcome inefficient expansion and persistence associated with existing universal CAR T cells;

(4) Improving target availability: exploring innovative technologies to enhance drug target availability and specificity of CAR T-cell therapy.

Technologies in these major research areas can be used to upgrade our existing product candidates as well as to generate future innovative pipeline product candidates. As of December 31, 2021, we had more than 300 patents of which more than 60 patents had been issued globally including China, the United States, Europe, and Japan. This is an increase of 31 issued patents and about 100 patent applications from the end of 2020. Our R&D activities would continue to generate substantial IP in our areas of expertise.

Manufacturing Capacity Expansion

We have established our in-house end-to-end clinical and commercial manufacturing capabilities for all three stages of CAR T manufacturing, including production of plasmids, lentiviral vectors and CAR T cells. With the clinical manufacturing facility in Xuhui, Shanghai and commercial GMP manufacturing facility in Jinshan, Shanghai ("**Jinshan Manufacturing Facility**"), we have been manufacturing CAR T cells in-house to support clinical trials in China and manufacturing the lentiviral vectors in-house to support clinical trials globally.

We have been expanding our manufacturing capacity in China and the U.S. to support both the clinical trials and the subsequent commercialization of our pipeline products. As of the date of this announcement, we successfully passed the official facility inspections and received the Certificate of Compliance from the City-County Inspections Department of Durham for our RTP CGMP manufacturing facility ("**RTP Manufacturing Facility**") in Durham, North Carolina. The RTP Manufacturing Facility will provide CARsgen with additional manufacturing capacity of autologous CAR T-cell products for 700 patients annually. The RTP Manufacturing Facility will support the Company's ongoing clinical studies and early commercial launch in North America and Europe. CARsgen has started building a world-class CMC team for the RTP manufacturing facility operations. The RTP Manufacturing Facility project adopted an integrated project delivery approach that greatly shortens construction turnaround time and improves cost effectiveness.

External License Agreement and Research Collaboration

CAFA Therapeutics, a subsidiary of CARsgen Therapeutics, has entered into a licensing agreement with HK inno.N Corporation (KOSDAQ: 195940) to develop and commercialize CT032 and CT053, for the potential treatment of various cancers in the Republic of Korea, with an upfront and additional milestone payments totaling up to USD50 million plus up to double-digit percentage royalties on net sales.

We also signed a new strategic agreement with Shanghai Cancer Institute for collaboration in oncology scientific and technologic research with the aim to enhance our understanding of oncology and technologies in CAR T-cell therapy and enrich our product pipeline.

I. MANAGEMENT DISCUSSION AND ANALYSIS

1. OVERVIEW

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 tumors. CARsgen has built an integrated cell therapy platform with in-house capabilities that span target discovery, 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 tumors, and reducing treatment costs.

Our product pipeline includes an upgraded fully human BCMA CAR T (CT053), a global potential first-in-class Claudin18.2 CAR T (CT041) which is the only CLDN18.2-targeted CAR T-cell product candidate that is being studied in clinical trials with IND approvals, and a global potential first-in-class GPC3 CAR T (CT011). We have obtained eight IND clearances for CAR T-cell therapies in China, the United States, and Canada ranking the first among all CAR T-cell therapy companies in China. Our vision is to become a global biopharmaceutical leader that brings innovative and differentiated cell therapies to cancer patients worldwide and make cancer curable.

During the Reporting Period, we have made significant advancements in the areas of clinical development of our pipeline products, innovation of technology advancement, expansion of manufacturing facilities, and establishment of external partnerships. Specifically, we made progress in the following areas:

Rapid clinical development of our product pipeline in China and overseas

CT053

For CT053, an autologous CAR T-cell product candidate against BCMA being developed for the treatment of R/R MM we have completed patient enrollment in our pivotal Phase II trial in China (LUMMICAR STUDY 1). Phase I of LUMMICAR STUDY 1 showed no dose limiting toxicities (DLT), no treatment-related deaths, and no Grade 3 or higher events of cytokine release syndrome (CRS). No patient developed immune effector cell-associated neurotoxicity syndrome (ICANS). At the cut-off date of July 8, 2021, the objective response rate (ORR) was 100% (14/14). Of these 14 patients, 78.6% (11/14) achieved stringent complete responses (sCR) with minimal residual disease (MRD) 10^{-5} negative, and 9 patients reached sustained CR/sCR for more than 12 months. The 12-month progression-free survival (PFS) rate was 85.7% (12/14). The median duration of response (mDOR) and the median progression-free survival (mPFS) had not been reached. For the patients without EMD, the CR/sCR rate was 91.7% (11/12) and the 12-month PFS rate reached 100%.

In North America, we have initiated our Phase 2 CT053 trial, CT053 LUMMICAR STUDY 2, after receiving feedback from the U.S. FDA. As communicated with the U.S. FDA, we are adding outpatient administration of CT053 into our U.S. clinical investigations. We treated our first patient in the Phase 2 trial in August 2021.

As of August 27, 2021, 27 patients received CT053 infusion in the Phase 1b portion of LUMMICAR STUDY 2. There was no DLT or treatment related death. No grade 3 or higher CRS was observed. One (3.7%) transient Grade 3 immune effector cell-associated neurotoxicity syndrome (ICANS) occurred and it was fully resolved after steroid administration. The overall response rate was 96.3% (26/27). Duration of response, progression free survival and overall survival had not been reached.

CARsgen plans to submit the NDA to the NMPA in the first half of 2022 and plans to submit the BLA to the U.S. FDA in 2023. The Company also plans to conduct additional clinical trials to develop CT053 as an earlier line of treatment for multiple myeloma.

CT041

CT041 is an autologous CAR T-cell product candidate against the protein CLDN18.2 and has the potential to be first-in-class globally. CT041 targets the treatment of CLDN18.2 positive solid tumors with a primary focus on gastric/gastroesophageal junction cancer (GC/GEJ) and pancreatic cancer (PC). Leveraging our in-depth understanding in CAR T-cell therapy, as well as our integrated antibody platform, we were the first in the world to successfully identify, validate, and report CLDN18.2 as a solid tumor-associated antigen for the potential development of CAR T-cell therapies for solid tumors. To further address the challenges of CAR T-cell therapies in treating solid tumors, we have developed an innovative patent-protected preconditioning regimen, or the FNC regimen, before infusion of CT041, which features the addition of low-dose nab-paclitaxel to the conventional regimen using cyclophosphamide and fludarabine for lymphodepletion.

CT041 has demonstrated promising therapeutic efficacy and safety in the ongoing investigator-initiated trial in China for CLDN18.2 positive gastric cancer and pancreatic cancer. As of the latest data cut-off date of April 8, 2021, a total of 37 patients, including 28 patients with GC/GEJ, 5 with pancreatic cancer, and 4 with other types of digestive system tumors, received CT041 infusion. 18 GC/GEJ patients who had failed at least 2 prior lines of therapies were treated at a dose of 2.5×10^8 CAR T cells (recommended phase II dose). An ORR of 61.1%, DCR of 83.3%, median PFS of 5.6 months, median DOR of 6.4 months, and median OS of 9.5 months with a median follow-up time of 7.6 months were achieved. PFS, OS and follow up duration were calculated from CAR T-cell infusion date. CT041 also showed preliminary efficacy in five evaluable patients with pancreatic cancer who failed at least two prior lines of systemic treatment. CT041 was generally well-tolerated with no Grade 3 or higher CRS or neurotoxicity was reported (approximately 95% of patients experienced CRS, all of which were grade 1 or 2). No treatment-related death or ICANS was reported.

CT041 is the only CLDN18.2-targeted CAR T-cell product candidate globally that is being studied in clinical trials with IND/CTA approvals from the FDA, the NMPA, and Health Canada. We have initiated the investigator-initiated trials, a Phase Ib clinical trial for advanced GC/GEJ and PC and a confirmatory Phase II clinical trial for advanced GC/GEJ in China, and initiated a Phase 1b clinical trial for advanced gastric or pancreatic adenocarcinoma in North America. CARsgen plans to submit an NDA to the NMPA in China in the first half of 2024 and also plans to initiate a Phase 2 clinical trial in the second half of 2022 in North America and to submit the BLA to the U.S. FDA in 2024.

Other Candidates

We are also on track in progressing other pipeline product candidates including (i) CT011, an autologous CAR T-cell product candidate against GPC3 being developed for the treatment of HCC. We have completed the enrollment of the Phase I trial in China; (ii) CT032, an autologous CAR T-cell products candidate against CD19 being developed for the treatment of B cell Non-Hodgkin's lymphoma. We are conducting a Phase I/II clinical trial in China; (iii) AB011, a humanized monoclonal antibody product candidate against CLDN18.2 and being developed for the treatment of CLDN18.2 positive solid tumors. We received supplemental application approval by the CDE regarding the addition of chemotherapy combination cohort with AB011 in Phase Ib, and we have subsequently initiated the combination cohort of AB011 with chemotherapy. We completed phase I monotherapy cohort enrollment and initiated combination with chemotherapy; and (iv) the IND-enabling or pre-clinical stage product candidates including CT0180, CT0181, KJ-C2111 (CT0590), KJ-C1807 (CT048), KJ-C2112, KJ-C2113 and KJ-C2114. We continue to drive the development and expect to submit IND applications as planned.

Continuous Discovery and Technology Development

Despite the approved CAR T-cell products for the treatment of terminal line hematologic malignancies, there are still significant challenges, such as limited efficacies against solid tumors, undesirable safety concerns, and high manufacturing and treatment costs. We strive to explore and develop innovative technology platforms to address these challenges to generate better cell therapy products to global cancer patients. Our main focus includes:

(1) Increasing efficacy against solid tumors: developing innovative technologies, such as our CycloCAR® technology, to enhance efficacies of CAR T cell against solid tumors. CycloCAR® is a next generation CAR T technology, which co-expresses cytokine IL-7 and chemokine CCL21 and potentially has greater clinical efficacy and reduced requirement for lymphodepletion conditioning;

(2) Enhancing safety profile: developing innovative technologies to minimize safety concerns including CRS/neurotoxicity/on-target off-tumor toxicities;

(3) Expanding patient accessibility: advancing our differentiated allogeneic THANK-uCAR® technology to reduce costs and increase affordability. THANK-uCAR® technology has the potential to overcome inefficient expansion and persistence associated with existing universal CAR T cells;

(4) Improving target availability: exploring innovative technologies that can potentially enhance drug target availability and specificity of CAR T-cell therapy. We developed Local Action Driven by Artificial Receptor (LADAR®) technology, in which the intracellular transcription of the gene of interest is controlled by a chimeric regulatory antigen receptor. Through the LADAR® artificial receptor, the intracellular activity is only triggered when the extracellular domain is activated upon binding to specific antigen, making it possible to precisely control when and where immune cells act against cancer cells.

These technologies are currently being developed in-house with global rights and can be used alone or combined to upgrade our existing product candidates as well as to generate future innovative pipeline product candidates.

As of December 31, 2021, we had more than 300 patents of which more than 60 patents had been issued globally including China, the United States, Europe and Japan. This is an increase of 31 issued patents and about 100 patent applications from the end of 2020. Our R&D activities would continue to generate substantial IP in our areas of expertise.

Manufacturing Capacity Expansion

We have established our in-house end-to-end clinical and commercial manufacturing capabilities for all three stages of CAR T manufacturing, including production of plasmids, lentiviral vectors, and CAR T cells. With the clinical manufacturing facility in Xuhui, Shanghai and commercial GMP manufacturing facility in Jinshan, Shanghai ("**Jinshan Manufacturing Facility**"), we have been manufacturing CAR T cells in-house to support clinical trials in China and manufacturing the lentiviral vectors in-house to support clinical trials globally.

We have been expanding our manufacturing capacity in China and the U.S. to support both the clinical trials and the subsequent commercialization of our pipeline products. As of the date of this announcement, we have made significant progress in the construction of RTP (Research Triangle Park) CGMP manufacturing facility ("**RTP Manufacturing Facility**") in Durham, North Carolina. We successfully passed the official facility inspections and received the Certificate of Compliance from the City-County Inspections Department of Durham. We have commenced commissioning, qualification, and validation of RTP Manufacturing Facility including the consultation with the FDA. Concurrently, we have been executing the technology transfer of CT053 and CT041 manufacturing process and analytical procedures to RTP Manufacturing Facility, advancing to the clinical manufacturing operations. The RTP Manufacturing Facility, with a total gross floor area of approximately 3,300 sq.m, will provide additional manufacturing capacity of autologous CAR T-cell products for 700 patients annually, and it will support the Company's ongoing clinical studies and early commercial launch in North America and Europe.

External License Agreement and Research Collaboration

In addition to the internal research and development activities, we are also actively seeking extensive collaborations with external partners. CAFA Therapeutics, a subsidiary of CARsgen Therapeutics, has entered into a licensing agreement with HK inno.N Corporation (KOSDAQ: 195940), a fully-integrated pharmaceutical company, to develop and commercialize CT032 and CT053, targeting CD19 and BCMA respectively, for the potential treatment of various cancers in the Republic of Korea. Under the terms of the agreement, CARsgen is entitled to receive an upfront payment and additional milestone payments totaling up to USD50 million as well as up to double-digit percentage royalties on net sales in the Republic of Korea. The collaboration with HK inno.N Corporation showcases our commitment to establishing more external partnerships with leading pharmaceutical companies to maximize the application of our technology platform and the value of our product pipeline to benefit more cancer patients globally.

On July 31, 2021, we reached a new agreement with Shanghai Cancer Institute, Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, for strategic collaboration in oncology research and technology development, following a previous agreement reached in 2015 between the two parties. This new agreement will accelerate the translation from early scientific research to clinical application for innovative cancer treatment options. This continued collaboration with Shanghai Cancer Institute will further enhance our understanding of technologies in CAR T-cell therapy and enrich our product pipeline.

Expansion and Retention of Talent

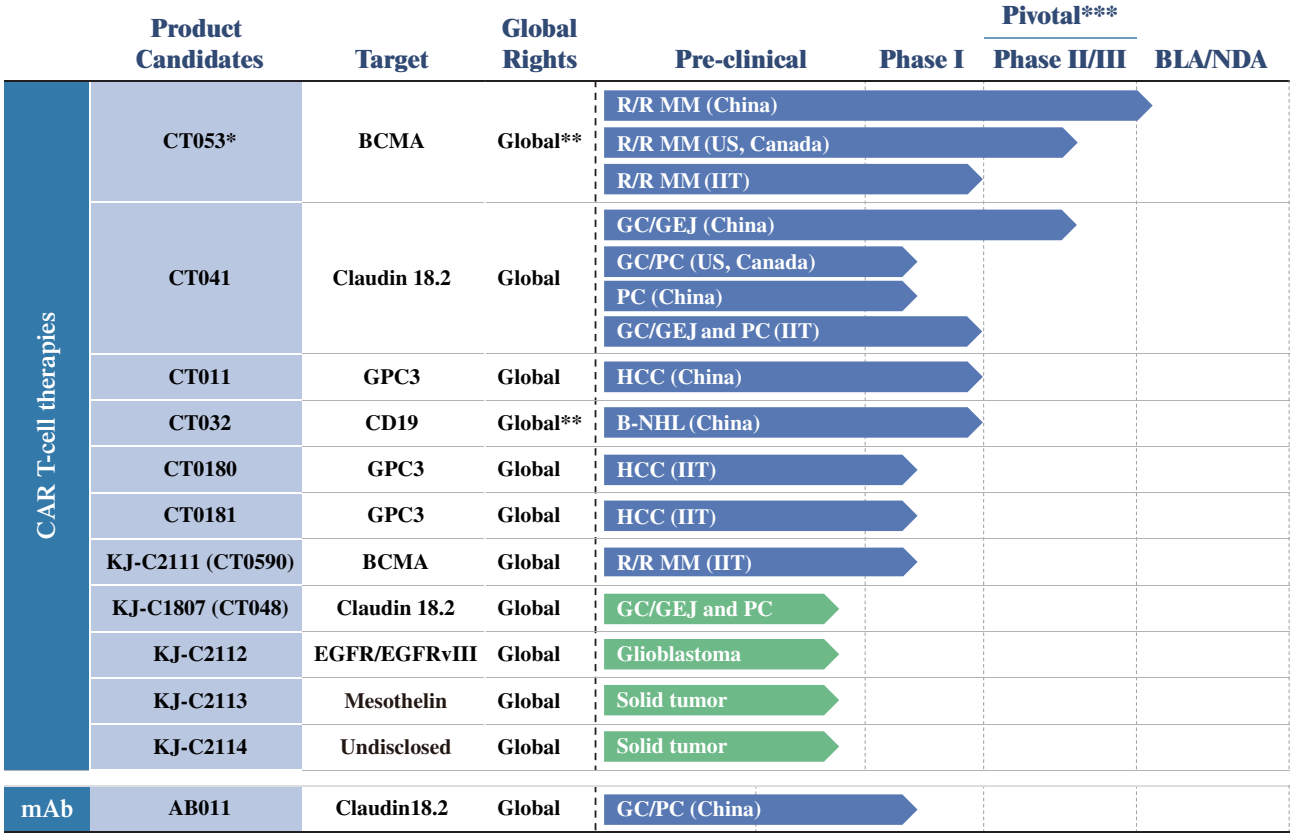
During the Reporting Period, we have expanded our team from about 337 employees as of December 31, 2020 to 573 employees as of December 31, 2021. We have also strengthened the leadership team. As of the date of this announcement, we have hired Mr. Richard John Daly as the President of CARsgen Therapeutics Corporation, a subsidiary of the Company in the U.S., reporting to Dr. Li Zonghai, Founder, Chairman of the Board, CEO, Chief Scientific Officer of CARsgen. Mr. Daly will lead the CARsgen US team for the international business activities of CARsgen outside of China, including clinical development, CMC operation, business development, commercialization, investor relations and public relations. Mr. Daly will also contribute to the overall growth strategies and business planning of CARsgen, helping the Company to develop more innovative and differentiated cell therapies to cancer patients worldwide and make cancer curable.

We have hired Dr. Chen Baolu as Senior Vice President of CMC Operation, responsible for the establishment and implementation of global CMC strategies. We have hired Ms. Jiang Caihua as Senior Vice President of Quality, responsible for the establishment and implementation of global quality management system for CARsgen. We have hired Dr. Zhou Guanjun as Vice President of Government Relations. Dr. Zhou is committed to monitoring policies and trends of biopharmaceutical industry and responsible for developing and strengthening relationships and communications with relevant government parties to support business development and strategic decisions for CARsgen China.

2. BUSINESS REVIEW

Our product and Product Pipeline

Since our inception, we have adopted and executed a strategic business model of self-developing innovative and differentiated biopharmaceutical products with a focus on CAR T-cell therapies. Within our pipeline, our Core Product Candidate, CT053, is for the treatment of R/R MM, a form of hematologic malignancy, and is at the most advanced development stage among our product candidates in our pipeline. In addition, CT041, CT011, and AB011 in our pipeline, are for the treatment of solid tumors, and in confirmatory Phase II, Phase I, and Phase Ib clinical trials, respectively. The following chart summarizes our pipeline and the development status of each product candidate as of the date of this announcement. Our product candidates are discovered and developed in-house, and we own the global rights to our product candidates. The clinical-stage product candidates are currently being developed for treating advanced stage cancers.



Notes:

* Core Product Candidate;

** Rights for the Republic of Korea market have been licensed out to HK Inno.N Corporation (KOSDAQ: 195940);

*** Phase II trials of some indications are pivotal studies;

R/R MM: relapsed/refractory multiple myeloma; GC: gastric cancer; PC: pancreatic cancer; B-cell non-Hodgkin lymphoma; GEJ: gastroesophageal junction cancer; HCC: hepatocellular carcinoma cancer.

Fully Human BCMA CAR T (CT053) — Our Core Product Candidate

CT053 is an upgraded fully human, autologous BCMA CAR T-cell product candidate for the treatment of R/R MM. It incorporates a CAR construct engineered by CARsgen that features a fully human BCMA-specific single-chain variable fragment with lower immunogenicity and increased stability, which reduces the self-activation of CAR T cells in the absence of tumor associated targets.

CARsgen has completed the patients enrollment of the pivotal Phase II trial patients in China (LUMMICAR STUDY 1) and plans to submit the NDA to the NMPA in the first half of 2022. CARsgen is conducting the pivotal Phase 2 trial in North America (LUMMICAR STUDY 2), and the Company plans to submit the BLA to the U.S. FDA in 2023. The Company also plans to conduct additional clinical trials to develop CT053 as an earlier line of treatment for multiple myeloma.

At the 2021 American Society of Hematology ("**ASH**") Annual Meeting, the Company presented two posters with study results for CT053 (an autologous CAR T-cell product candidate against BCMA), which include (1) the sustainable efficacy and safety results from the Phase I/II study in China (LUMMICAR-1), and (2) an integrated analysis in patients with R/R MM by high-risk factors.

A total of 14 heavily pretreated patients received CT053 infusion in the Phase I LUMMICAR STUDY 1. No DLT, no treatment-related deaths, and no Grade 3 or higher events of CRS were observed. No patient developed ICANS. At the cut-off date of July 8, 2021, the ORR was 100% (14/14). Of these 14 patients, 78.6% (11/14) achieved sCR with MRD 10^{-5} negative, and 9 patients reached sustained CR/sCR for more than 12 months. 92.9% (13/14) of patients achieved at least very good partial responses (VGPR). The 12-month PFS rate was 85.7% (12/14). The mDOR and the mPFS had not been reached. For the patients without extramedullary disease (EMD), the CR/sCR rate was 91.7% (11/12) and the 12-month PFS rate reached 100%, which demonstrate better treatment trends.

Our Investigator initiated trials (IITs) were initiated in September 2017. A total of 24 heavily pretreated patients received CT053 BCMA CAR T-cell infusion. No treatment-related death and no Grade 3 or higher events of CRS were observed. One patient developed Grade 3 neurotoxicity (convulsion) which resolved quickly. The ORR and CR/sCR were 87.5% and 79.2%, respectively. As of June 30, 2021, with a median follow-up time of 14.8 months, the DOR and PFS were 21.8 months (95%CI, 9.2-NR) and 18.8 months (95%CI, 10.1-NR), respectively. The PFS rate at 24 months was 42.4%. Eight patients are still in remission and in long-term follow-up.

CT053 represents a promising treatment option for patients with R/R MM, including patients with high-risk disease, and it is generally well-tolerated. A total of 38 patients (IITs and LUMMICAR STUDY 1) received CT053 infusions. Of these, 31.6% of patients had EMD, 50.0% of patients had high-risk cytogenetics, and 28.9% of patients had ISS stage III disease. Based on the results of the analysis stratified by high-risk factors, the CR/sCR rate, mPFS, and mDOR were 58.3%, 9.3 months, and 9.2 months in patients with EMD, whereas the measures in patients without EMD were 88.5%, 25.0 months, and 24.0 months, respectively. The mPFS and mDOR in patients with high-risk cytogenetics were 15.6 months and 18.3 months, and were both 13.3 months in ISS III patients, while mPFS and mDOR had not been reached in patients without these two high-risk factors. These results suggest that the presence of the high-risk disease characteristics of EMD, high-risk cytogenetics, and ISS stage III at baseline might affect the clinical benefits. Although there were 50% of patients with high-risk disease at baseline, in the 13.9 months median follow-up time, the ORR was 92.1% (35/38), with 78.9% (30/38) of patients achieving CR/sCR and 86.8% (33/38) of patients achieving at least VGPR, and the mPFS and mDOR were 22.7 months and 24.0 months respectively.

In North America, we have initiated our Phase 2 CT053 trial of LUMMICAR STUDY 2. As communicated with the U.S. FDA, we are adding outpatient administration of CT053 into our U.S. clinical investigations. We treated our first patient in the Phase 2 trial in August 2021.

As of August 27, 2021, 27 patients received CT053 infusion in the Phase 1b portion of LUMMICAR STUDY 2. There was no DLT and no treatment related death. No Grade 3 or higher CRS was observed. One (3.7%) transient Grade 3 ICANS occurred and it fully resolved after steroid administration. The ORR was 96.3% (26/27). The mPFS, mDOR and mOS had not been reached.

Additional data from these clinical trials are planned to be disclosed in academic journals or conferences.

CARsgen has developed CT053 in-house with our integrated research and development platform. CT053 has received Regenerative Medicine Advanced Therapy (RMAT) and Orphan Drug designations for the treatment of R/R MM from the U.S. FDA in 2019, PRIority MEdicines (PRIME) eligibility and Orphan Medicinal Product designation for the treatment of R/R MM from the EMA in 2019 and 2020, respectively, and Breakthrough Therapy designation for the treatment of R/R MM from the NMPA in 2020.

We believe that CT053, the BCMA CAR T-cell product candidate with an upgraded, fully human CAR, has a promising efficacy profile and a favorable safety profile, as evidenced by the absence of Grade 3 or higher CRS and no treatment-related patient deaths in the investigator-initiated trials and the Phase I clinical trials.

WE MAY NOT BE ABLE TO ULTIMATELY MARKET CT053 SUCCESSFULLY.

Humanized CLDN18.2 CAR T (CT041)

CT041 is an autologous CAR T-cell product candidate against the protein CLDN18.2 and has the potential to be first-in-class globally. CT041 targets the treatment of CLDN18.2 positive solid tumors with a primary focus on gastric/gastroesophageal junction cancer and pancreatic cancer. CLDN18.2 is expressed in a range of different solid tumors, including gastric/gastroesophageal junction cancer, pancreatic, colorectal, lung, and ovarian cancers. Leveraging our in-depth understanding in CAR T-cell therapy, as well as our integrated antibody platform, we were the first in the world to successfully identify, validate, and report CLDN18.2 as a solid tumor-associated antigen for the potential development of CAR T-cell therapies for solid tumors in which CLDN18.2 is prevalently or highly expressed. To further address the challenges of CAR T-cell therapies in treating solid tumors, we have developed an innovative preconditioning regimen, or the FNC regimen, before infusion of CT041, which features the addition of low-dose nab-paclitaxel to the conventional regimen using cyclophosphamide and fludarabine for lymphodepletion.

CT041 is the only CLDN18.2-targeted CAR T-cell product candidate globally that is being studied in clinical trials with IND/CTA approvals from the FDA, the NMPA, and Health Canada. We have initiated the investigator-initiated trials, a Phase Ib clinical trial for advanced GC/GEJ and PC and a confirmatory Phase II clinical trial for advanced GC/GEJ in China, and initiated a Phase 1b clinical trial for advanced gastric or pancreatic adenocarcinoma in North America. CARsgen plans to submit an NDA to the NMPA in China in the first half of 2024 and also plans to initiate a Phase 2 clinical trial in the second half of 2022 in North America and to submit the BLA to the U.S. FDA in 2024.

CT041 has demonstrated promising therapeutic efficacy and safety in the ongoing investigator-initiated trial, which is led by Dr. Lin Shen at the Beijing Cancer Hospital.

At the European Society for Medical Oncology Congress 2021 ("**ESMO Congress 2021**"), we have orally presented updates on the investigator-initiated trial of CT041. As of April 8, 2021, 37 patients received CT041 infusion and completed at least 12 weeks of evaluation, including 28 cases of gastric/gastroesophageal junction cancer (GC/GEJ), 5 cases of pancreatic cancer (PC) and 4 cases of other types of digestive system tumors. Approximately 84% of patients had received at least 2 prior lines of therapies and the median number of metastatic organs was 3.

For the 28 patients with GC/GEJ, 67.9% of the patients had peritoneal metastases. 42.9% and 35.7% of the patients had been exposed to anti-PD-(L)1 antibody and multikinase inhibitor respectively.

Within the 28 patients with GC/GEJ, 18 received at least 2 prior lines of therapies. 18 GC/GEJ patients who had failed at least 2 prior lines of therapies (including 8 (44% of) patients had exposed to an anti-PD-(L)1 antibody) were treated at a dose of 2.5×10^8 (recommended phase II dose) CAR T cells and achieved an ORR of 61.1%, DCR of 83.3%, median PFS of 5.6 months, median DOR of 6.4 months, and median OS of 9.5 months with a median follow-up of 7.6 months. PFS, OS and follow up duration were calculated from CAR T-cell infusion date.

For the 28 patients with GC/GEJ, a subgroup analysis revealed that ORR could be maintained at 50% or above in patients with different baseline characteristics, such as expression level of CLDN18.2 and previous anti-PD-(L)1 antibody treatment. See the following table for details:

	Number of patients	ORR
CLDN18.2 expression		
High expression (≥2+, ≥ 70%)	19	57% (37.2, 75.5)
Medium expression (≥2+, ≥40% and < 70%)	7	58% (33.5, 79.7)
Low expression (+ or < 40%)	2	50% (1.3, 98.7)
Previous anti-PD-(L)1 antibody treatment		
Unreceived	16	63% (35.4, 84.8)
Received	12	50% (21.1, 78.9)
Peritoneal Metastasis		
Yes	19	58% (33.5, 79.7)
No	9	56% (21.2, 86.3)
WHO Classification		
Signet ring cell carcinoma	12	58% (27.7, 84.8)
Others	15	60% (32.3, 83.7)
Lauren Classification		
Intestinal	10	70% (34.8, 93.3)
Diffused/Mixed	16	50% (24.7, 75.3)

CT041 also showed preliminary efficacy in five evaluable patients with pancreatic cancer who failed at least 2 prior lines of systemic treatment. Additional data from this clinical trial are planned to be disclosed in academic journals or conferences.

CT041 was generally well-tolerated with no Grade 3 or higher CRS and no neurotoxicity reported (approximately 95% of patients experienced CRS, all of which were grade 1 or 2). No treatment-related death and no ICANS were reported. The CT041 cells were observed to persist in the peripheral blood for eight weeks and up to six months and achieve T cell expansion up to several to tens of thousands of CAR copies in blood per microgram of genomic DNA.

In North America, we have initiated our Phase 1b trial of CT041-ST-02. We have treated the first patient in July 2021.

In 2020 and 2021, CT041 received Orphan Drug designation from the U.S. FDA for the treatment of GC/GEJ and Orphan Medicinal Product designation from the EMA for the treatment of advanced gastric cancer. In November 2021, CT041 was granted PRIME eligibility by the EMA for the treatment of advanced gastric cancer. In January 2022, CT041 was granted Regenerative Medicine Advanced Therapy (RMAT) Designation for the treatment of advanced gastric or gastroesophageal junction adenocarcinoma with CLDN18.2 positive tumors.

We believe CT041 has the potential to fulfill the significant unmet clinical needs for the treatment of gastric and pancreatic cancer and serve as a proof-of-concept for our breakthrough technology to apply CAR T modality to treating solid tumors.

WE MAY NOT BE ABLE TO ULTIMATELY MARKET CT041 SUCCESSFULLY.

Humanized GPC3 CAR T (CT011)

CT011 is a CAR T-cell product candidate with proof-of-concept clinical data for the treatment of HCC and has the potential to be the first-in class globally. Our co-founder, CEO and Chief Scientific Officer, Dr. Li Zonghai led the world's first successful effort in identifying, validating and reporting GPC3 as a tumor-associated target for the development of CAR T-cell therapies to treat HCC. Our investigator-initiated trial in China enrolled 13 patients with advanced GPC3+ HCC and demonstrated that CT011 therapy was generally tolerable in patients who have been heavily pretreated. The overall survival rates at 6 months, 1 year and 3 years were 50.3%, 42.0% and 10.5%, respectively, with a median overall survival of 278 days. We have completed enrollment of a Phase I trial in China.

Humanized CD19 CAR T (CT032)

CT032 is an autologous CAR T-cell product candidate against CD19 being developed for the treatment of B cell NHL. CT032 incorporates a humanized CD19-specific single-chain fragment variant, which we expect to reduce the toxicity of CT032 and reduce immunogenicity, as compared to currently commercialized CD19-specific CAR T-cell products which use murine anti-CD19 single chain variable fragment as the targeting moiety. We are conducting an open-label, single arm, Phase I/II trial in China to evaluate the safety and tolerability of CT032.

Anti-CLDN18.2 mAb (AB011)

AB011 is a humanized monoclonal antibody product candidate that targets CLDN18.2, which is a stomach-specific isoform of Claudin-18 and is highly expressed in gastric and pancreatic cancer cells. AB011 displayed strong in vitro antitumor activities against CLDN18.2 positive tumor cells in antibody-dependent cellular cytotoxicity (ADCC) assays and complement-dependent cytotoxicity (CDC) assays and showed potent in vivo antitumor activities when combined with oxaliplatin and 5-fluorouracil in CLDN18.2 positive gastric cancer mouse models. We obtained the second IND clearance in the world for a mAb targeting CLDN18.2. We are conducting a Phase I clinical trial of AB011 for the treatment of CLDN18.2 positive solid tumors in China to evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy of AB011 injection.

In the second quarter of 2021 we received supplemental application approval by the CDE regarding the addition of chemotherapy combination cohort with AB011 in Phase Ib, and we have subsequently initiated the combination cohort of AB011 with chemotherapy. We completed phase I monotherapy cohort enrollment and initiated combination with chemotherapy. In the monotherapy phase, we observed that one patient with advanced gastric cancer who had failed previous second-line chemotherapy achieved a CR. During the combination treatment phase, the first two patients with advanced gastric cancer were assessed to be in PR at week 6 after the first dose.

We plan to consult with the NMPA in the second half of 2022 and to initiate the subsequent Phase II clinical trial.

IND-Enabling or Pre-Clinical Stage Product Candidates

In addition to the above clinical-stage product candidates which are in IND trials, we have internally developed seven IND-enabling or pre-clinical stage product candidates as described below.

CT0180 is an autologous T cell product engineered to express a fusion protein of GPC3-targeted antibody fused T cell receptor (aTCR). It consists of a single-chain variable fragment (scFv) targeting GPC3 and a CD3ε subunit, which can form a functional TCR complex with other TCR subunits (TCRα, TCRβ, CD3γ, CD3δ and CD3ζ) and redirect T cells to kill tumor cells in an MHC-independent manner. Our preclinical studies have shown that CT0180 could effectively recognize and kill GPC3-positive hepatocellular carcinoma cells and significantly inhibit HCC tumor growth in mouse xenograft models with reduced cytokine release compared to GPC3-CAR T cells in vitro and in vivo, which improve the safety and applicability of adoptive cell therapies. IIT trial has been initiated in China to evaluate the efficacy and safety of CT0180 in the treatment of hepatocellular carcinoma.

CT0181 is an autologous T cell product engineered with GPC3-targeted antibody fused T cell receptor co-expressing IL-7 cytokine. It consists of a single-chain variable fragment (scFv) targeting GPC3 and a CD3ε subunit which can form a functional TCR complex with other TCR subunits (TCRα, TCRβ, CD3γ, CD3δ and CD3ζ) and redirect T cells to kill tumor cells in an MHC-independent manner. Co-expressed IL-7 via a 2A peptide is a cytokine that could enhance the proliferation and survival of T cells. Our preclinical studies have shown that CT0181 displays superior antitumor efficacy, T cell persistence, and immunological memory in solid tumors xenografts with low cytokine release compared to GPC3-CAR T cells. IIT trial has been initiated in China to evaluate the efficacy and safety of CT0181 in the treatment of hepatocellular carcinoma.

KJ-C2111 (CT0590) is an allogeneic CAR T-cell product candidate deploying our THANK-uCAR® technology that targets BCMA. We are developing KJ-C2111 for the treatment of R/R MM. We have initiated IIT trial to evaluate the efficacy and safety of CT0590 for the treatment of R/R MM.

KJ-C1807 (CT048) is a next-generation autologous CAR T-cell product candidate developed with our CycloCAR® technology. We anticipate that by co-expressing cytokine IL-7 and chemokine CCL21, KJ-C1807 potentially has a greater clinical efficacy and reduced requirement for lymphodepletion conditioning. KJ-C1807 targets CLDN18.2 and is being developed to treat patients with gastric/gastroesophageal junction cancer and pancreatic cancer.

KJ-C2112 is a next-generation autologous EGFR/EGFRvIII-bitargeted CAR T-cell product candidate harboring a humanized single-chain antibody with single specificity that binds to an epitope present on wild-type EGFR – and EGFRvIII-overexpressing tumor cells, but not on EGFR-expressing normal cells. KJ-C2112 is armored with a transcription factor. Pre-clinical studies have demonstrated the efficacy of KJ-C2112, such as its ability to suppress growth of EGFR-and/or EGFRvIII-overexpressing glioma xenografts in mice and prolong the survival of tumor-bearing mice. Therefore, KJ-C2112 may be a promising modality for the treatment of patients with EGFR/EGFRvIII-overexpressing glioblastoma. We plan to collaborate with an experienced reputable principal investigator and further study KJ-C2112 in an investigator-initiated trial.

KJ-C2113 is a next-generation autologous CAR T-cell product candidate developed with our CycloCAR® technology that targets mesothelin, a tumor differentiation antigen normally restricted to the body's mesothelial surfaces, but significantly overexpressed in a broad range of solid tumors. We are developing KJ-C2113 for the treatment of various types of solid tumors.

KJ-C2114 is an allogeneic CAR T-cell product candidate deploying our THANK-uCAR® technology with an undisclosed target for the treatment of certain solid tumors.

Discovery and Pre-clinical Research

We have established an integrated research and development platform covering the full CAR T development cycle including target discovery, antibody development, vector design, manufacturing, quality assurance, and quality control. Our integrated cell therapy platform is composed of target discovery, hybridoma and antibody humanization platform, fully human phage display antibody library platform, antibody identification platform, immune cell function evaluation platform, plasmid and lentiviral vector preparation platforms, cell therapy process development platform, analytical platforms with molecular, flow cytometry, biochemical, physical-chemical, and cell-based analytical capabilities, biological samples tests platform, clinical-scale and commercial-scale CAR T manufacturing platform, and platform for clinical studies. This platform enables us to efficiently and effectively advance a product candidate from early discovery to clinical trials and potentially to commercialization.

We continue to dedicate ourselves to advancing innovative CAR T technologies to address the major challenges of the industry.

To enhance the efficacy against solid tumors, we continue to develop next generation CAR T technologies, such as CycloCAR®. CycloCAR® is featured by co-expression of cytokines IL-7 and chemokine CCL21 in the CAR T cells to potentially improve clinical efficacy and reduce the requirement of lymphodepletion conditioning. Our preclinical studies have shown that IL-7 could enhance the proliferation and survival of CAR T cells and inhibit the apoptosis of CAR T cells, and CCL21 could drive infiltration of T cells and dendritic cells into tumor sites. The CycloCAR T cells could improve the therapeutic effects against solid tumors in mice when compared with conventional CAR T cells. Moreover, even without preconditioning chemotherapy, the CycloCAR T cells could potently suppress the tumor growth with a significantly better efficacy than CAR T cells co-expressing IL-7 and CCL19 (7×19 CAR T, a previously reported design by other researchers). Taken together, our studies demonstrated that, independent of lymphodepletion chemotherapy, CycloCAR T cells exert potent antitumor effects which are facilitated by infiltration of T cells and dendritic cells into tumor tissues, increase in survival of CAR T cells, as well as the potential anti-angiogenesis effect. We are using CycloCAR® to develop CAR T-cell therapies against several different targets including CLDN18.2, GPC3 and mesothelin. We continue to explore potential combination approaches to boost the therapeutic effects of single agents and identify new targets and approaches to tackle new indications.

To minimize the safety concerns, we continue to develop innovative technologies that can help reduce the CRS, neurotoxicity and on-target off-tumor toxicities. We are able to leverage our own antibody platform, powered by a fully human phage display library and improved hybridoma technology, to identify and optimize antibody fragments with higher specificity for tumor targets and increased stability, which lead to reduced auto-activation of CAR T cells in the absence of tumor targets and controlled level of cytokine release. As a proof-of-concept of our antibody engineering capabilities, we have developed CT053, which had not induced Grade 3 or higher CRS in the investigator-initiated trials or in the Phase I clinical trials and allowed less administration of anti-IL-6 medication and other immunosuppressant mediation as of the respective data cutoff date of the ongoing investigator initiated trials and clinical trials. We continue to explore other innovative technologies to improve the safety profiles of CAR T cells while maintaining or enhancing the anti-tumor effects.

To reduce the cost and increase the accessibility of CAR T-cell therapies, we continue to develop our differentiating allogeneic THANK-uCAR® technology. THANK-uCAR® is our proprietary technology to generate allogeneic CAR T cells with improved expansion and persistence by modifying donor-derived T cells. To minimize graft versus host disease (GvHD) and host versus graft response (HvGR) from allogeneic T cells, we disrupt the genomic loci encoding T cell receptor (TCR) and β2 microglobulin (B2M) to eliminate surface expression of the TCR or the human leukocyte antigen (HLA), an approach that has been validated by previous research. However, NK cells attack T cells without HLA expression, which then limits the expansion and persistence of the allogeneic CAR T cells. To protect the allogeneic CAR T cells from the patient's NK cells, we arm the TCR^-/HLA^- CAR T cells with a CAR that recognizes NKG2A to eliminate the NKG2A positive NK cells and therefore resist the attack by NK cells. Our in vitro and in vivo studies demonstrated that the armoring the TCR^-/HLA^- CAR T cells with anti-NKG2A CAR resulted in improved expansion in the presence of NK cells. We are developing allogeneic CAR T-cell product candidates using THANK-uCAR® technology, which we believe could potentially increase CAR T cell expansion, persistence and efficacy. We believe the successful application of THANK-uCAR® technology would significantly lower the cost of CAR T-cell therapy and eventually increase patient accessibility.

In the development of cancer therapies, the non-specific expression of tumor associated antigens poses a significant challenge, as these antigens are also expressed in normal tissues, leading to the on-target off-tumor toxicities. To resolve the challenge with target availability, we continue to explore innovative technologies to enhance drug target availability and therefore make undruggable targets druggable. We developed LADAR® technology, in which the intracellular transcription of the gene of interest is controlled by a chimeric regulatory antigen receptor. Through the LADAR® artificial receptor, the intracellular activity is only triggered when the extracellular domain is activated upon binding to specific antigen, making it possible to precisely control when and where immune cells act against cancer cells.

The LADAR-CAR circuits require both antigens for LADAR® and CAR recognition to kill target cells and thus reduce on-target off-tumor effects since these two antigens are not simultaneously expressed in normal tissues. In our in vitro studies, LADAR® system induced strong gene expression in response to antigen engagement and importantly, nearly no leakage expression in resting cells. LADAR-CAR T cells executed killing function only if both the antigens presented.

We are also working on other applications of LADAR® system, such as LADAR-cytokine circuits. We believe that the establishment of LADAR® system is the key step to develop the CAR T cells with powerful and precise killing of cancer.

To develop effective CAR T-cell products for more cancer types and further enhance the anti-tumor effect, we have been expanding our research to more promising oncology targets for cell therapies. In addition, leveraging our proprietary antibody platforms, we have successfully developed humanized or fully-human antibodies against these targets, such as GPRC5D, B7-H3, etc. These antibodies, together with our CAR-T technology platforms, will help further enhance the product pipeline.

Utilizing these technologies, we strive to further enrich our product pipeline and subsequently progress to these pipeline product candidates clinical and commercial stage.

As of December 31, 2021, we had more than 300 patents of which more than 60 patents had been issued globally including China, the United States, Europe and Japan. This status is an increase of 31 issued patents and about 100 patent applications from the end of 2020. Our R&D activities would continue to generate substantial IP in our areas of expertise.

Manufacturing

We have established in-house GMP-compliant manufacturing capabilities to support end-to-end CAR T manufacturing, including plasmids, lentiviral vectors and CAR T cells production. Our clinical manufacturing facility in Xuhui, Shanghai with a total gross floor area, or GFA, of approximately 3,000 sq.m. and an annual CAR T production capacity to support the CAR T-cell treatment of 200 patients has been used for clinical manufacturing of CAR T-cell products in supporting multiple clinical studies of our leading assets. Since establishment, our Xuhui facility has achieved over 95% manufacturing success rate for all product candidates.

We have also completed the construction of our commercial-scale manufacturing facility located in Jinshan, Shanghai with a total GFA of approximately 7,600 sq.m. and an estimated manufacturing capacity to support CAR T-cell treatment of up to 2,000 patients annually. The Jinshan Manufacturing Facility passed the on-site inspection conducted by the Shanghai Medical Products Administration, or the SHMPA, and obtained the first Manufacture License for Pharmaceutical Products ("**Manufacturing License**") issued in China for CAR T-cell therapy.

With the clinical manufacturing facility in Xuhui, Shanghai and the commercial manufacturing facility in Jinshan, Shanghai, we can produce the lentiviral vectors and CAR T cells in-house to support clinical trials and CAR T cells commercialization in China. We also provide the lentiviral vectors to the clinical trials outside of China.

We have made significant progress in the construction of CARsgen RTP Manufacturing Facility in Durham, North Carolina. We successfully passed the official inspections and received the Certificate of Compliance from the City-County Inspections Department of Durham. We have commenced commissioning, qualification, and validation of RTP Manufacturing Facility including the consultation with the FDA. Meanwhile, we have been executing the technology transfer of CT053 and CT041 manufacturing process and analytical procedures to RTP Manufacturing Facility, advancing to the operations of clinical manufacturing.

The RTP Manufacturing Facility, with a total gross floor area of approximately 3,300 sq.m, will provide CARsgen with additional manufacturing capacity of autologous CAR T-cell products for 700 patients annually. The RTP Manufacturing Facility will support the Company's ongoing clinical studies and early commercial launch in North America and Europe. CARsgen has started building a world-class CMC team for the RTP manufacturing facility operations. The RTP Manufacturing Facility project adopted an integrated project delivery approach that greatly shortens construction turnaround time and improves cost effectiveness. This project has received the Job Development Investment Grant (JDIG) award and other investment incentives from North Carolina state, Durham County and Durham City.

To accelerate the clinical production at the RTP Manufacturing Facility, CARsgen Jinshan Manufacturing Facility in Shanghai, China will continue to provide the lentiviral vector used in manufacturing of CAR T-cell products for CT053 and CT041 clinical studies under active INDs cleared by the U.S. FDA. CARsgen has established sustainable and scalable GMP manufacturing capacity of lentiviral vectors. The large-scale production of lentiviral vector at Jinshan Manufacturing Facility could significantly reduce the manufacturing costs of CAR T-cell products.

By building end-to-end manufacturing capabilities in-house, we expect to significantly increase manufacturing sustainability, reduce manufacturing costs, and shorten the vein-to-vein time. In addition, we have an in-house GMP-compliant manufacturing facility capable of high yield production of lentiviral vectors. Our Jinshan, Shanghai facility has been allowed by the U.S. FDA to provide lentiviral vectors for manufacturing our CT041 and CT053 cell products in support of U.S. clinical trials. With large scale lentiviral vectors production, we could greatly reduce the CAR T manufacturing costs.

Commercialization

To better prepare for the commercialization of our innovative CAR T-cell products, we have started to formulate our marketing strategies in a staggered approach corresponding to the expected launch timeline of our product candidates. The staggered approach features stepwise expansion of our future marketing efforts. We have established a marketing team for the pre-launch activities of CT053 and CT041. For the China market, with NDA submission for CT053 expected in the first half of 2022, we intend to cover key Class III Grade A hospitals that are equipped to administer CT053 CAR T-cell therapy in their hematology department in tier one cities and selected tier two cities. We also plan to broaden our footprint into oncology departments as we approach the launch of CT041 and other solid tumor product candidates.

We aim to establish a centralized collaborative system for standard clinical management of CAR T-cell therapies by partnering with local key research and clinical centers, in order to achieve a whole-process management of patients treatment including medical evaluation, apheresis, pre-treatment, CAR T-cell infusion, post-infusion monitoring and long-term follow-up. We may also pursue a national CAR T consortia model by engaging with reputable medical centers and key opinion leaders to set up regional CAR T-cell treatment centers, as a mean to re-allocate the scarce medical resources from large cities to less-developed cities or regions and thereby provide access to patients who otherwise may not receive CAR T-cell treatment. In addition, in order to ensure continuous, efficient and cost-effective supplies of CAR T-cell products for commercial use, we aim to establish a standard validation process to expedite the establishment and certification of GMP-compliant CAR T manufacturing centers. We will also develop our commercial capabilities for overseas markets such as the United States and Europe.

Expansion and Retention of Talent

During the Reporting Period, we have expanded our team from about 337 employees as of December 31, 2020 to 573 employees as of December 31, 2021 of whom 64.6% are female. We have also strengthened the leadership team. As of the date of this announcement, we have hired Mr. Richard John Daly as the President of CARsgen Therapeutics Corporation, reporting to Dr. Li Zonghai, Founder, Chairman of the Board, CEO and Chief Scientific Officer of CARsgen. Mr. Daly will lead the CARsgen US team for the international business activities of CARsgen outside of China, including clinical development, CMC operation, business development, commercialization, investor relations and public relations. Mr. Daly will also contribute to the overall growth strategies and business planning of CARsgen, helping the Company to develop more innovative and differentiated cell therapies to cancer patients worldwide and make cancer curable. Details of the biography of the senior management are set out in the Directors and Senior management section of the annual report of the Company for the year ended December 31, 2021.

We have hired Dr. Chen Baolu as Senior Vice President of CMC Operation, responsible for the establishment and implementation of global CMC strategies. We have hired Ms. Jiang Caihua as Senior Vice President of Quality, responsible for the establishment and implementation of global quality management system for CARsgen. We have hired Dr. Zhou Guanjun as Vice President of Government Relations. Dr. Zhou is committed to monitoring policies and trends of biopharmaceutical industry, and responsible for developing and strengthening relationships and communication with relevant government parties to support business development and strategic decisions for CARsgen China.

Other Corporate Development

CAFA Therapeutics, a subsidiary of CARsgen Therapeutics, entered into a licensing agreement with HK inno.N Corporation (KOSDAQ: 195940), a fully-integrated pharmaceutical company, to develop and commercialize CT032 and CT053, targeting CD19 and BCMA respectively, for the potential treatment of various cancers in the Republic of Korea. Under the terms of the agreement, CARsgen will receive an upfront and additional milestone payments totaling up to USD50 million as well as up to double digit royalties on net sales in the Republic of Korea. This collaboration with HK inno.N Corporation (KOSDAQ: 195940) showcases our commitment to establishing more external partnerships with leading pharmaceutical companies to maximize the application of our technology platform and value of our product pipeline to benefit more cancer patients globally.

On July 31, 2021, we reached a new agreement with Shanghai Cancer Institute, Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, for strategic collaboration in oncology research and technology development, following a previous agreement reached in 2015 between the two parties. This continued collaboration with Shanghai Cancer Institute will further enhance our understanding of oncology research and technologies in CAR T-cell therapy and enrich our product pipeline.

Impact of COVID-19

The COVID-19 outbreak since the end of 2019 has not caused termination of our clinical trials and has had a slight impact on our patient enrollment, patient visits and monitor's hospital visits. To minimize the impact of COVID-19, we conducted clinical trials at multiple institutions located in different areas, cities and countries. Although some delays have occurred due to lack of hospital staff and slight delays in responses from health authorities, there was no significant impact on the progress of clinical trials and interactions with health authorities. We do not expect the COVID-19 outbreak to have any material long-term impact on our clinical trials or our overall clinical development plans. Moreover, we continuously monitor and assess the impact of pandemic on the Company's U.S. operations and business activities outside China. We have noticed the manageable impacts of COVID-19 pandemic on the operations of the U.S. medical sites and the external vendors, which are involved in our clinical studies outside China. We may virtually monitor and audit some medical sites, CDMOs and CROs due to the temporary suspension of onsite visits by our partners. The procurement and delivery of materials, reagents and equipment that are used in the clinical manufacturing may be delayed or cancelled due to global supply chain constraints. Those uncertainties described above may slow down the progress of our clinical programs in the future. We have also noticed a potential impact of the COVID-19 pandemic on the construction, commissioning, qualification and validation of our U.S. CGMP manufacturing facility in Durham, North Carolina. The overall timeline of U.S. facility construction and commencement remains on track.

In 2021, the Company implemented a set of COVID-19 prevention and control measures, and there is no significant impact on our daily work and domestic travel for business. The measures undertaken include daily monitoring of the pandemic, tracking workforce health and travelling information, ensuring vaccination of the workforce, distributing personal protective equipment, frequent disinfection and good ventilation at workplace, and implementing strict visitor policies.

Although the pandemic remains ongoing, we believe the pandemic will not significantly impact our ability to continue our operations. While we cannot predict exactly how our operations will be affected, we do not expect to have any long-term impact on our business due to the COVID-19 outbreak.

Industry Overview

As a novel treatment modality, CAR T-cell therapy offers breakthough efficacy and curative potential for cancer patients. The global CAR T-cell therapy market has been experiencing strong growth since the approval of the first CAR T-cell therapy in 2017. The global CAR T-cell therapy market is further driven by the increases in global cancer incidence, the approval of more CAR T-cell therapies in more cancer types and indications, the improvements in manufacturing technology and capacities, and the availability of CAR T-cell products in more markets. As of the date of this announcement, there are six CAR T-cell products approved by U.S. FDA and two CAR T-cell products approved by NMPA in China. However, there are still significant unmet medical needs for the cancer patients worldwide, calling for more and better innovative CAR T-cell products, particularly for the treatment of solid tumors. With our pipeline products, including CT053 and CT041, and innovative technology platforms, including CycloCAR®, THANK-uCAR® and LADAR®, we are committed to developing the innovative therapies to fulfill these unmet medical needs.

Future and Outlook

With the mission of "making cancer curable", we will continue to develop innovative product candidates for the treatment of cancer patients worldwide. Building on the milestones we have achieved, we will focus on rapid clinical development of CT053 and CT041 in both China and overseas. We will continue to advance the other product candidates in clinical and pre-clinical stages and to develop innovative CAR T technologies to further optimize the efficacy, safety and affordability of the CAR T-cell products. We will continue to expand our manufacturing capacity in China and the United States to support the clinical trials and future commercialization of our product candidates and to make CAR T-cell treatments more accessible and affordable. We will continue to establish additional external partnerships with leading research institutes and pharmaceutical companies on technology and product licenses as means to maximize the application of our technology platform and the value of our product pipeline, bringing more innovative cell therapy products to cancer patients worldwide and ultimately creating more value for our investors and the society.

3. FINANCIAL REVIEW

Overview

We have no products approved for commercial sale and have not generated any revenue from product sales. We have never been profitable and have incurred operating losses in every year since inception, with operating losses of RMB574 million and RMB327 million for the years ended December 31, 2021 and 2020, respectively. Substantially all of our operating losses resulted from research and development expenses and administrative expenses.

Loss for the years

Net loss was RMB4,744 million for the year ended December 31, 2021, representing an increase of RMB3,680 million from RMB1,064 million for year ended December 31, 2020. The increase was primarily due to (i) the increase of the Fair Value Loss, which totaled RMB4,156 million for the year ended December 31, 2021, representing an increase of RMB3,432 million from RMB724 million for the year ended December 31, 2020. Fair value loss related financial instruments were converted to ordinary shares upon the completion of the IPO, hence no loss would be recognized after the IPO; (ii) the Listing Fees of approximately RMB27 million for the year ended December 31, 2021, representing an increase of RMB23 million from RMB4 million for the year ended December 31, 2020; (iii) the share-based compensation, which totaled RMB14 million for the year ended December 31, 2021, representing an increase of RMB12 million from RMB2 million for the year ended December 31, 2020; and (iv) higher research and development expenses and higher administrative expenses.

Non-IFRS Measures

To supplement the Group's consolidated net loss and net loss per share which are presented in accordance with the IFRS, the Company has provided adjusted net loss and adjusted net loss per share as additional financial measures, which are not required by, or presented in accordance with, the IFRS.

Adjusted net loss for the periods and adjusted net loss per share for the periods represent the net loss and net loss per share respectively excluding the effect of certain non-cash items and/or one-time events, namely the fair value loss of the financial instrument issued to investors, the listing fee and share-based compensation. The terms adjusted net loss and adjusted net loss per share are not defined under the IFRS.

The table below sets forth a reconciliation of the loss to adjusted loss during the years indicated:

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
	(Audited)	(Audited)
Loss for the years	**(4,744,423)**	(1,064,049)
Add:		
Fair value loss of financial instrument issued to investors	**4,155,572**	724,287
Listing fee	**26,580**	4,323
Share-based compensation	**13,504**	1,714
Adjusted net loss	**(548,767)**	(333,725)

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
	(Audited)	(Audited)
Loss per share for the years	**(12.26)**	(5.37)
Add:		
Fair value loss of financial instrument issued to investors per share	**10.74**	3.66
Listing fee per share	**0.07**	0.02
Share-based compensation per share	**0.03**	0.01
Adjusted net loss per share	**(1.42)**	(1.68)

The Company believes that the adjusted non-IFRS measures are useful for understanding and assessing the underlying business performance and operating trends, and that the Company's management and investors may benefit from referring to these adjusted financial measures in assessing the Group's financial performance by eliminating the impact of certain unusual, non-recurring, non-cash and/or non-operating items that the Group does not consider indicative of the performance of the Group's core business. These non-IFRS measures, as the management of the Group believes, is widely accepted and adopted in the industry in which the Group is operating in. However, the presentation of these non-IFRS measures is not intended to be considered in isolation or as a substitute for the financial information prepared and presented in accordance with the IFRS. Shareholders of the Company and potential investors should not view the adjusted results on a stand-alone basis or as a substitute for results under IFRS. And these non-IFRS measures may not be comparable to similarly-titled measures represented by other companies.

Research and Development Expenses

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
	(Audited)	(Audited)
Testing and clinical expenses	**204,309**	124,269
Employee benefit expenses	**178,297**	76,717
Research and development consumables	**53,456**	30,240
Depreciation of property, plant and equipment	**28,155**	25,490
Depreciation of right-of-use assets	**16,193**	7,459
Utilities	**10,875**	9,436
Amortization of intangible assets	**5,321**	5,494
Travelling and transportation expenses	**2,982**	1,668
Office expenses	**776**	–
Short term lease and low value lease expenses	**691**	719
Professional service fees	**240**	–
Other expenses	**426**	260
Total	**501,721**	**281,752**

Research and development expenses increased to RMB502 million for the year ended December 31, 2021, representing an increase of RMB220 million from RMB282 million for the year ended December 31, 2020, primarily due to increased head count and staff cost and expenses for testing and productions in support of our clinical trials.

Administrative Expenses

	Year ended December 31,	
	2021	**2020**
	RMB'000	*RMB'000*
	(Audited)	(Audited)
Employee benefit expenses	**57,138**	20,427
Listing expenses	**26,580**	4,323
Professional service fees	**23,260**	34,021
Office expenses	**10,013**	7,455
Auditors' remuneration	**3,793**	1,100
– audit service	**3,585**	600
– non-audit service	**208**	500
Depreciation of property, plant and equipment	**1,492**	1,302
Travelling and transportation expenses	**799**	405
Amortization of intangible assets	**679**	364
Depreciation of right-of-use assets	**606**	–
Utilities	**308**	75
Short term lease and low value lease expenses	**100**	–
Other expenses	**1,063**	7,421
Total	**125,831**	**76,893**

Administrative expenses increased to RMB126 million for the year ended December 31, 2021, representing an increase of RMB49 million from RMB77 million for the year ended December 31, 2020, primarily due to listing expenses incurred in relation to the Company's IPO and increased headcount and staff cost.

Details of employee benefit expenses and share-based payments included in the above administrative and research and development expenses are as below:

Employee benefit expenses

	Year ended December 31,	
	2021	**2020**
	RMB'000	*RMB'000*
	(Audited)	(Audited)
Wages and salaries	**178,613**	83,703
Pension costs	**13,020**	7,124
Share-based compensation	**13,504**	1,714
Other employee benefits	**30,298**	4,603
Total	**235,435**	**97,144**
Amount included in Research and Development Expenses	**178,297**	76,717
Amount included in Administrative Expenses	**57,138**	20,427

The increase of employee benefit expenses is mainly due to higher headcount and the related increase in staff salary and benefit costs. The larger increase of pension costs is due to social security relief policy of COVID-19 in 2020.

Share-based payments

Expenses for the share-based compensation have been charged to the consolidated statements of comprehensive loss as follows:

	Year ended December 31,	
	2021	**2020**
	RMB'000	*RMB'000*
	(Audited)	(Audited)
Administrative expenses	**1,890**	411
Research and development expenses	**11,614**	1,303
Total	**13,504**	**1,714**

Fair Value Loss of Financial Instruments Issued to Investors

The fair value loss of financial instruments issued to investors increase to RMB4,156 million for the year ended December 31, 2021, representing an increase of RMB3,432 million from RMB724 million for the year ended December 31, 2020, primarily due to the steeper increase in the fair value of the financial instruments leading up to our IPO. The financial instruments were converted to ordinary shares upon the Company's IPO in June 2021, hence no loss would be recognized after the IPO.

4. LIQUIDITY AND CAPITAL RESOURCES

Management monitors and maintains a level of cash and cash equivalents deemed adequate to finance our operations and mitigate the effects of fluctuations. In addition, management monitors our borrowings and, from time to time, evaluates operations to renew our borrowings upon expiry based on our actual business requirements. We rely on equity financing and debt financing as our major sources of liquidity.

The following table sets forth our cash flows for the periods indicated:

	For the year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
	(Audited)	(Audited)
Net cash used in operating activities	**(512,322)**	(295,150)
Net cash used in investing activities	**(2,471,321)**	(6,897)
Net cash generated from financing activities	**2,674,032**	1,302,473
Net (decrease)/increase in cash and cash equivalents	**(309,611)**	1,000,426
Cash and cash equivalents at beginning of the period	**1,042,969**	96,476
Exchange loss on cash and cash equivalents	**(42,074)**	(53,933)
Cash and cash equivalents at end of the period	**691,284**	1,042,969

Net Cash Used in Operating Activities

During the Reporting Period, we incurred negative cash flows from operations, and substantially all of our operating cash outflows resulted from our research and development expenses and administrative expenses.

Our operating activities used RMB512 million and RMB295 million for the year ended December 31, 2021 and 2020, respectively. We are currently a pre-income company. We believe our pipeline products have promising global market potential in the future. We intend to continue investing in our research and development efforts and aim to obtain marketing approvals for our product candidates as soon as feasible. As we launch and commercialize our product candidates, we expect to generate operating income and improve our net operating cash outflow position.

Net Cash Used in Investing Activities

Our cash used in investing activities mainly reflects our cash used for investing in short term deposits and our purchase of property, plant and equipment. For the year ended December 31, 2021, our net cash used in investing activities was RMB2,471 million, which was primarily attributable to investment of term deposit and purchase of equipments. For the year ended December 31, 2020, our net cash used in investing activities was RMB7 million, which was primarily attributable to purchase of equipment.

Net Cash Generated from Financing Activities

During the Reporting Period, we derived our cash inflow from financing activities primarily from proceeds from the IPO, issuance of financial instruments to investors and bank borrowings.

For the year ended December 31, 2021, our net cash generated from financing activities was RMB2,674 million, primarily attributable to proceeds from our IPO of RMB2,576 million and net proceeds from bank borrowings of RMB146 million. For the year ended December 31, 2020, our net cash generated from financing activities was RMB1,302 million, which was primarily attributable to issuance of financial instruments to investors.

Cash and Cash Equivalents and Term Deposits with Original Maturity over Three Months

	As at December 31, 2021 ***RMB'000*** **(Audited)**	As at December 31, 2020 *RMB'000* (Audited)
Cash at banks		
– RMB	**33,773**	121,393
– USD	**657,511**	921,576
Subtotal	**691,284**	**1,042,969**
Term deposits with original maturity between three and twelve months – USD	**2,315,654**	–
Total	**3,006,938**	**1,042,969**

The Group's cash and cash equivalents and term deposits with original maturity between three and twelve months as at December 31, 2021 were RMB3,007 million, representing an increase of RMB1,964 million compared to RMB1,043 million as at December 31, 2020. The increase was primarily attributable to the net proceeds from the IPO.

Borrowing and Gearing Ratio

The Group's total borrowings, including interest-bearing borrowings, as at December 31, 2021 were RMB227 million, representing an increase of RMB147 million compared to RMB80 million as at December 31, 2020.

As at December 31, 2021 and December 31, 2020, the Group's bank borrowings of approximately RMB12 million and RMB16 million respectively are pledged by property, plant and equipment and right-of-use assets of the Group.

The fair values of the borrowings approximate their carrying amounts as the discounting impact is not significant.

As at December 31, 2021, the Group's unsecured borrowings are mature within six to twelve months with the interest rate ranging between 3.5000% – 5.5000% (2020: 3.5000% – 5.5000%)

As at December 31, 2021, the Group's secured borrowings is mature within three years with the interest rate of 5.2250% (2020: 5.2250%). The gearing ratio (calculated by dividing the sum of borrowings and lease liabilities by total equity) of the Group as at December 31, 2021 was 11.28%. Gearing ratio as at December 31, 2020 is not applicable as it would lead to a negative number.

Lease liabilities

The Group leases land use right and properties. Lease on land use right has been fully paid and lease on properties were measured at net present value of the lease payments to be paid during the lease terms.

Lease liabilities were discounted at incremental borrowings rates of the Group.

Our lease liabilities increased to RMB111 million as at December 31, 2021 from RMB20 million as at December 31, 2020, due to newly rented plant, offices and staff dormitories.

5. OTHER FINANCIAL INFORMATION

Significant Investments, Material Acquisitions and Disposals

As at December 31, 2021, we did not hold any significant investments. During the year ended December 31, 2021, we did not have material acquisitions or disposals of subsidiaries, associates and joint ventures.

Foreign Exchange Risk

We have transactional currency exposures. Certain of our bank balances, other receivables, and accruals and other payables are dominated in foreign currencies and are exposed to foreign currency risk. We currently do not have a foreign currency hedging policy. However, our management monitors foreign exchange exposure and will consider appropriate hedging measures in the future should the need arise.

Capital Expenditure

For the year ended December 31, 2021, the Group's total capital expenditure amounted to approximately RMB178 million, which was used in purchase of property, plant and equipment, and software.

Charge on Assets

As at December 31, 2021 and 2020, the Group's building with carrying values of RMB33 million and RMB35 million respectively were pledged for certain of the Group's borrowings.

As at December 31, 2021 and December 31, 2020, the Group's land use right with carrying values of RMB6.8 million and RMB6.9 million respectively was pledged as collateral for the Group's borrowings.

Contingent Liability

As at December 31, 2021, the Group did not have any material contingent liabilities.

Employees and Remuneration Policies

During the Reporting Period, we have expanded our team from about 337 employees as at December 31, 2020 to 573 employees as at December 31, 2021. As at December 31, 2021, we had a total of 573 employees, with 64.6% of them are female.

In compliance with the applicable labor laws, we enter into standard confidentiality and employment agreements with our key management and research staff. The contracts with our key personnel typically include a standard non-compete agreement that prohibits the employee from competing with us, directly or indirectly, during his or her employment and for up to two years after the termination of his or her employment. The agreements also typically include undertakings regarding assignment of inventions and discoveries made during the course of his or her employment.

During the Reporting Period and up to the date of this announcement, we did not experience any strikes, labor disputes or industrial action which had a material effect on our business. We believe we have not experienced any significant difficulty in recruiting staff for our operations. We have established a labor union that represents employees with respect to the promulgation of bylaws and internal protocols in China.

Our employees' remuneration consists of salaries, bonuses, share-based incentive plans, social insurance contributions and other welfare payments. In accordance with applicable laws, we have made contributions to social insurance funds (including pension plan, unemployment insurance, work-related injury insurance, medical insurance and maternity insurance, as applicable) and housing funds for our employees. During the Reporting Period and up to the date of this announcement, we had complied with all statutory social insurance fund obligations applicable to us under PRC & US laws in all material aspects, and housing fund obligations applicable to us under PRC laws.

To remain competitive in the labor market, we provide various incentives and benefits to our employees. We invest in continuing education and training programs, including internal and external training, for our management staff and other employees to upgrade their skills and knowledge. We also provide competitive salaries, project and stock incentive plans to our employees, especially key employees.

Future Investment Plans and Expected Funding

The Group will continue to expand its markets in the PRC and globally in order to tap its internal potential and maximize shareholders' interest. The Group will continue to grow through self-development, mergers and acquisitions, and other means. We will employ a combination of financing channels to finance capital expenditures, including but not limited to internal funds and bank loans. Currently, the bank credit lines available to the Group are adequate.

II. ANNUAL RESULTS

CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME
FOR THE YEAR ENDED DECEMBER 31, 2021

	Note	Year ended December 31, 2021 RMB'000	2020 RMB'000
Revenue	3	**25,813**	–
Cost of sales		**–**	–
Gross profit		**25,813**	–
Administrative expenses	6	**(125,831)**	(76,893)
Research and development expenses	6	**(501,721)**	(281,752)
Other income	4	**21,793**	9,977
Other gains – net	5	**6,041**	21,623
Operating loss		**(573,905)**	(327,045)
Finance income	7	**3,568**	763
Finance costs	7	**(10,869)**	(13,480)
Finance costs – net		**(7,301)**	(12,717)
Fair value changes in financial instruments issued to investors		**(4,155,572)**	(724,287)
Loss before income tax		**(4,736,778)**	(1,064,049)
Income tax expense	8	**(7,645)**	–
Loss for the year and attribute to the equity holders of the Company		**(4,744,423)**	(1,064,049)
Other comprehensive (loss)/income for the year:			
Items that may be reclassified to profit or loss			
Exchange differences on translation of subsidiaries		**20,312**	55,683
Items that will not be reclassified to profit or loss			
Exchange differences on translation of the Company		**(11,328)**	29,024
Fair value changes relating to financial instruments issued to investors due to the Company's own credit risk		**(25,093)**	34,104
Other comprehensive (loss)/income for the year, net of tax		**(16,109)**	118,811
Total comprehensive loss for the year and attribute to the equity holders of the Company		**(4,760,532)**	(945,238)
Loss per share for the loss attributable to owners of the Company			
Basic and diluted loss per share (in RMB)	9	**(12.26)**	(5.37)

CONSOLIDATED STATEMENT OF FINANCIAL POSITION

AS AT DECEMBER 31, 2021

	Note	**As at December 31, 2021**	As at December 31, 2020
		RMB'000	*RMB'000*
ASSETS			
Non-current assets			
Property, plant and equipment		**300,898**	129,630
Right-of-use assets		**85,291**	27,139
Intangible assets		**20,133**	23,521
Other non-current assets and prepayments		**28,460**	17,766
		434,782	198,056
Current assets			
Deposits and other receivables	*10*	**41,885**	2,418
Other current assets and prepayments		**22,030**	10,408
Term deposits with original maturity between three and twelve months		**2,315,654**	-
Cash and cash equivalents		**691,284**	1,042,969
		3,070,853	1,055,795
Total assets		**3,505,635**	1,253,851
EQUITY AND LIABILITIES			
Equity attributable to the equity holders of the Company			
Share capital	*11*	**1**	-
Reserves		**2,996,659**	(1,676,128)
Total equity/(deficit)		**2,996,660**	(1,676,128)

	Note	As at December 31, 2021 *RMB'000*	As at December 31, 2020 *RMB'000*
LIABILITIES			
Non-current liabilities			
Financial instruments issued to investors		**-**	2,745,584
Borrowings	*14*	**7,375**	11,981
Lease liabilities		**97,312**	14,016
Deferred income		**15,116**	13,167
		119,803	2,784,748
Current liabilities			
Lease liabilities		**14,027**	5,890
Accruals and other payables	*13*	**138,025**	67,379
Current income tax payable		**7,645**	-
Deferred income		**10,144**	3,591
Borrowings	*14*	**219,331**	68,371
		389,172	145,231
Total liabilities		**508,975**	2,929,979
Total equity and liabilities		**3,505,635**	1,253,851

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

1. GENERAL INFORMATION

CARsgen Therapeutics Holdings Limited (hereinafter the "Company") was incorporated under the law of Cayman Islands as a limited liability company on 9 February 2018. The address of the Company's registered office is P.O. Box 31119 Grand Pavilion, Hibiscus Way, 802 West Bay Road, Grand Cayman, KY1-1205 Cayman Islands.

The Company is an investment holding company. The Company and its subsidiaries (hereinafter collectively referred to as the "Group") are a global clinical-stage biopharmaceutical company discovering, researching and developing cell therapies in the People's Republic of China (the "PRC") and United States of America (the "US").

The Company's shares began to list on the Main Board of The Stock Exchange of Hong Kong Limited (the "Stock Exchange") on June 18, 2021 (the "Listing").

The consolidated financial statements are presented in thousands of Renminbi ("RMB"), unless otherwise stated, and were approved and authorized for issue by the Board of Directors of the Company on March 22, 2022.

2. BASIS OF PREPARATION

The consolidated financial statements of the Group have been prepared in accordance with International Financial Reporting Standards ("**IFRSs**") issued by International Accounting Standards Board ("**IASB**") and disclosure requirements of the Hong Kong Companies Ordinance ("**HKCO**"). The consolidated financial statements have been prepared under the historical cost convention, as modified by the revaluation of financial assets and liabilities at fair value through profit or loss, which are carried at fair value.

(i) New and amended standards adopted by the Group

The Group has applied the following amendments for the first time for their annual reporting period commencing January 1, 2021:

- Amendments to IFRS 16, Covid-19-Related Rent Concessions
- Amendments to IFRS9, IAS39, IFRS7, IFRS4 and IFRS16 Interest Rate Benchmark Reform-phase 2

The amendments listed above did not have any impact on the amounts recognized in prior periods and are not expected to significantly affect the current or future periods.

The following new standards and amendments to existing standards have been issued but are not yet effective for the annual period after January 1, 2021 and which the Group has not early adopted.

(ii) New standards and interpretation not yet adopted

Standards	Key requirements	Effective for annual periods beginning on or after
IFRS 17	Insurance Contracts	January 1, 2023
Amendments to IFRS 17		January 1, 2023
Amendments to IAS 1	Classification of Liabilities as Current or Non-current	January 1, 2023
Amendments to IAS 16	Property, plant and equipment: Proceeds before intended use	January 1, 2022
Amendments to IAS 37	Onerous contract – cost of fulfilling a contract	January 1, 2022
Annual improvements	Annual improvements to IFRS standards 2018-2020	January 1, 2022
Amendments to IFRS 10 and IAS 28	Sale or contribution of assets between an investor and its associate or joint venture	To be determined
Amendments to IFRS 3	Reference to the Conceptual Framework	January 1, 2022
Amendments to IAS 1 and IFRS Practice Statement 2	Disclosure of Accounting Policies	January 1, 2023
Amendments to IAS 8	Definition of Accounting Estimates	January 1, 2023

The Group has already commenced an assessment of the impact of these new or revised standards and amendments, certain of which are relevant to the Group's operations. According to the preliminary assessment made by the directors, these standards and amendments are not expected to have a significant impact on the Group's financial performance and position.

3. REVENUE

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
Revenue from customers recognised at a point in time		
License fee	**25,813**	–

4. OTHER INCOME

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
Government grants	**14,513**	9,977
Interest income on term deposits with original maturity between three and twelve months	**6,043**	–
Others	**1,237**	–
Total	**21,793**	9,977

5. OTHER GAINS – NET

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
Net foreign exchange gains	**7,451**	21,623
Others	**(1,410)**	–
Total	**6,041**	21,623

6. EXPENSE BY NATURE

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
Employee benefit expenses	**235,435**	97,144
Testing and clinical expenses	**204,309**	124,269
Research and development consumables	**53,456**	30,240
Depreciation of property, plant and equipment	**29,647**	26,792
Listing expenses through statement of comprehensive income	**26,580**	4,323
Professional service expenses	**23,500**	34,021
Depreciation of right-of-use assets	**16,799**	7,459
Utilities	**11,183**	9,511
Office expenses	**10,789**	7,455
Amortization of intangible assets	**6,000**	5,858
Auditors' remuneration	**3,793**	1,100
– Audit service	**3,585**	600
– Non-audit service	**208**	500
Travelling and transportation expenses	**3,781**	2,073
Short term lease and low value lease expenses	**791**	719
Other expenses	**1,489**	7,681
Total	**627,552**	358,645

7. FINANCE COSTS – NET

	Year ended December 31,	
	2021	2020
	RMB'000	*RMB'000*
Finance Income		
Interest income	**3,568**	763
Finance costs		
Interest expense on lease liabilities	**(2,846)**	(376)
Interest expense on loans with conversion option	**–**	(10,095)
Interest expense on bank borrowings	**(8,023)**	(3,009)
Total finance cost	**(10,869)**	(13,480)
Total finance costs – net	**(7,301)**	(12,717)

8. INCOME TAX EXPENSE

	Year ended December 31	
	2021	2020
	RMB'000	*RMB'000*
Current income tax		
– PRC corporate income tax	**–**	–
– Ireland capital gains tax	**7,645**	–
Deferred income tax	**–**	–
	7,645	–

Current income tax

The Group is subject to income tax on an entity basis on profits arising in or derived from the jurisdictions in which members of the Group are domiciled and operated.

(a) Cayman Islands income tax

The Company was incorporated in the Cayman Islands as an exempted company with limited liability under the Companies Law of the Cayman Islands and accordingly, is exempted from Cayman Islands income tax.

(b) Hong Kong income tax

No provision for Hong Kong profits tax has been provided for at the rate of 16.5% as the Company has no estimated assessable profit.

(c) PRC corporate income tax

Subsidiaries in Mainland China are subject to income tax at a rate of 25% pursuant to the Corporate Income Tax Law of the PRC and the respective regulations (the "CIT Law"), with the exception of CARsgen Therapeutics (Shanghai) obtained its High and New Technology Enterprises status in year 2020 and hence is entitled to a preferential tax rate of 15% for a three-year period commencing 2020.

No provision for PRC corporate income tax was provided for, as there's no assessable profit.

(d) US corporate income tax

CARsgen USA, which was incorporated in Delaware, the United States on May 4, 2016, was subject to statutory U.S. Federal corporate income tax at a rate of 21% for the year ended December 31, 2021 and 2020. CARsgen USA was also subject to the state income tax for the years ended December 31, 2021 and 2020.

No provision for US corporate income tax was provided for as there's no assessable profit.

(e) British Virgin Islands income tax

Under the current laws of BVI, the subsidiary incorporated in BVI is not subject to tax on income or capital gains. In addition, upon payments of dividends by our BVI subsidiaries to us, no BVI withholding tax is imposed.

(f) Ireland corporation income tax and Ireland capital gains tax

Subsidiary in Ireland is subject to income tax at a rate of 12.5% on the estimated assessable profit and 33% on the capital gains. Provision for Ireland capital gain tax has been provided as the subsidiary has realized capital gain for the year ended December 31, 2021.

9. LOSS PER SHARE

(a) Basic loss per share

Basic loss per share is calculated by dividing the loss of the Group attributable to the equity holders of the Company by weighted average number of ordinary shares outstanding during the periods.

	Year ended December 31,	
	2021	2020
Loss attributable to the ordinary equity holders of the company (RMB'000)	**(4,744,423)**	(1,064,049)
Weighted average number of ordinary shares in issue (in thousand)	**386,835**	198,140
Basic loss per share (RMB)	**(12.26)**	(5.37)

(b) Diluted loss per share

Diluted loss per share is calculated by adjusting the weighted average number of ordinary shares outstanding to assume conversion of all dilutive potential ordinary shares. For the years ended December 31, 2021 and 2020, the Company had three categories of potential ordinary shares including: loans with conversion option, financial instruments issued to investors and share-based payments. As the Group incurred losses for the years ended December 31, 2021 and 2020, the potential ordinary shares were not included in the calculation of diluted loss per share as their inclusion would be anti-dilutive. Accordingly, diluted loss per share for the years ended December 31, 2021 and 2020 are the same as basic loss per share of the respective periods.

10. DEPOSITS AND OTHER RECEIVABLES

	As at December 31, 2021	As at December 31, 2020
	RMB'000	*RMB'000*
Lease incentive receivables	**32,660**	–
Deposits – current	**5,298**	1,813
Others	**3,927**	605
Total	**41,885**	2,418

None of the above assets is past due. The financial assets included in the above balances related to deposits and other receivables for which there was no history of default and the expected credit losses are considered minimal.

The maximum exposure to credit risk at the reporting date is the carrying value of receivables mentioned above.

The carrying amounts of the Group's deposits and other receivables approximate their fair values.

11. SHARE CAPITAL

Authorized:

	Number of shares *In thousands*	Nominal value of shares *USD*	RMB equivalent value *RMB'000*
As at January 1, 2020	50,000,000	50,000	349
Share subdivision *(Note (a))*	150,000,000	–	–
As at December 31, 2020	200,000,000	50,000	349
As at January 1, 2021 and December 31, 2021	200,000,000	50,000	349

Issued and fully paid:

	Number of ordinary shares at USD0.00000025 par value *In thousands*	RMB equivalent value *RMB'000*
As at January 1, 2021	**198,140**	–*
Issue of shares held in trust *(Note (b))*	**19,623**	–*
Conversion of Preferred Shares to Ordinary Shares upon Global Offering *(Note (c))*	**254,837**	1
Issue of shares by Global Offering *(Note (d))*	**94,747**	–*
Share option scheme *(Note (e))*	**190**	–*
As at December 31, 2021	**567,537**	1

* The amounts are less than RMB1,000.

Note (a): On September 11, 2020, the Company issued 2,476,745 ordinary shares to YIJIE Biotech BVI at par value of USD0.000001.

On September 11, 2020, the Company underwent a subdivision of shares whereby the Company's authorized share capital of USD50,000 was amended by re-designation from 50,000,000,000 ordinary shares at USD0.000001 par value each into 200,000,000,000 ordinary shares at USD0.00000025 par value each. Accordingly, the issued 49,534,883 shares were divided into 198,139,532 shares.

Note (b): On May 11, 2021, the Company allotted and issued 12,497,947 Shares to Carfa Unity Limited and 7,125,575 Shares to Carfe Unity Limited, both of which were wholly-owned by the 2019 Equity Incentive Plan Trustee. Such Shares are to be held in trust by the 2019 Equity Incentive Plan Trustee to facilitate the transfer of Shares to the grantees upon vesting of the relevant Share Options and Share Awards. The Shares of the Company held in Carfa Unity Limited and Carfe Unity Limited were accounted as "Reserve-Treasury shares held in trust".

Note (c): All 254,836,638 preferred shares were automatically converted into ordinary shares at HK$32.8 per share upon the completion of Global Offering. The difference between HK$32.8 and the par value of each share were capitalized as "Reserve-Share premium". In addition, the cumulative fair value changes due to credit risk related to the preferred shares were transferred from other reserve to accumulated losses on the same date.

Note (d): In connection with the Company's listing, 94,747,000 ordinary shares of the Company at US$0.00000025 par value each were issued at HK$32.8 per share for a total cash consideration of HK$3,107,701,000 (equivalent to RMB2,576,082,000) on June 18, 2021. Netting off underwriting commissions and other issuance costs through equity with the amount of RMB88,349,000, the Group received RMB2,487,733,000. Excluding the par value, the amount was recorded as "Reserve-Share premium".

Note (e): During the year ended December 31, 2021, the Company issued 190,390 shares at the cost of HKD1,278,699 (equivalent to RMB1,118,000 approximately) as certain employees of the Group exercised their options under 2019 Stock Option Scheme ("2019 Plan").

12. DIVIDEND

No dividend was declared or paid by the Company or the companies now comprising the Group during the year ended December 31, 2021 and 2020.

13. ACCRUALS AND OTHER PAYABLES

	As at December 31, 2021 *RMB'000*	As at December 31, 2020 *RMB'000*
Accrued expenses	**45,520**	33,903
Payables for acquisition of property, plant and equipment	**37,969**	2,244
Payables for research and development consumables	**340**	2,367
Staff salaries and welfare payables	**45,837**	20,825
Listing expenses payables	**–**	5,190
Other taxes payables	**2,620**	1,805
Interest payables	**393**	209
Others	**5,346**	836
Total	**138,025**	67,379

14. BORROWINGS

	As at December 31, 2021 *RMB'000*	As at December 31, 2020 *RMB'000*
Non-current		
Secured bank borrowings	**7,375**	11,981
Current		
Unsecured borrowings	**214,727**	64,000
Secured bank borrowings	**4,604**	4,371
	219,331	68,371
Total	**226,706**	80,352

III. CORPORATE GOVERNANCE RELATED INFORMATION

Purchase, Sale or Redemption of the Company's Listed Securities

Neither the Company nor any of its subsidiaries purchased, sold or redeemed any of the Company's listed securities during the Relevant Period.

Model Code for Securities Transactions

The Company has adopted the Model Code set out in Appendix 10 to the Listing Rules. Specific enquiries have been made to all Directors and the Directors have confirmed that they have complied with the Model Code for the Relevant Period.

The Company's employees, who are likely to be in possession of inside information of the Company, have also been subject to the Model Code for securities transactions. No incident of non-compliance of the Model Code by the employees was noted by the Company for the Relevant Period.

Compliance with the Corporate Governance Code

The Company has adopted and applied the principles and code provisions as set out in the Corporate Governance Code contained in Appendix 14 to the Listing Rules. For the Relevant Period, the Company has complied with the mandatory code provisions in the Corporate Governance Code, except for the deviation from code provision C.2.1 and C.5.1 as explained below.

Pursuant to code provision C.2.1 of the Corporate Governance Code, companies listed on the Stock Exchange are expected to comply with, but may choose to deviate from the requirement that the roles of chairman and chief executive should be separate and should not be performed by the same individual. We do not have separate Chairman of the Board and CEO and Dr. Li Zonghai ("**Dr. Li**"), the Chairman of our Board and CEO, currently performs these two roles. Our Board believes that, in view of his experience, personal profile and his roles in our Company as mentioned above, Dr. Li is the Director best suited to identify strategic opportunities and focus of the Board due to his extensive understanding of our business as our CEO. Our Board also believes that the combined role of Chairman of the Board and CEO can promote the effective execution of strategic initiatives and facilitate the flow of information between management and the Board. Our Board will continue to review and consider splitting the roles of Chairman of the Board and the CEO at a time when it is appropriate by taking into account the circumstances of our Group as a whole.

Pursuant to code provision C.5.1, the Board should meet regularly and board meetings should be held at least four times a year at approximately quarterly intervals. There are approximately six months from the Listing Date to December 31, 2021, so board meetings should be held at least two times during the Relevant Period. In view of the simplicity of the Group's businesses, we only convened one board meeting during the Relevant Period, on which the interim results of the Group for the six months ended June 30, 2021 were reviewed and discussed by the Directors. Together with the circulation of written materials to keep the Board informed throughout the Relevant Period, sufficient measures had been taken to ensure that there was efficient communication among the Directors, including the independent non-executive Directors.

The Board will continue to review and monitor the code of corporate governance practices of the Company with an aim to maintaining a high standard of corporate governance.

Subsequent Event

Save as disclosed in this announcement, as at the date of this announcement, the Group has no significant events occurred after the Reporting Period which require additional disclosures or adjustments.

Legal Proceedings

As of December 31, 2021, as far as the Company is aware, the Company and its subsidiaries were not involved in any material litigation or arbitration and no material litigation or claim of material importance was pending or threatened against or by the Company.

Use of Proceeds from the Global Offering

The Company's Shares were listed on the Stock Exchange on June 18, 2021 with a total of 94,747,000 offer shares issued and the net proceeds raised from the Global Offering were approximately HK$3,008 million. The net proceeds from the Listing (adjusted on a pro rata basis based on the actual net proceeds) have been and will be utilized in accordance with the purposes set out in the Prospectus. There is no change in the intended use of net proceeds as previously disclosed in the Prospectus as follows:

- approximately HK$902.4 million (US$115.7 million) (or approximately 30% of the net proceeds) to fund further development of our Core Product Candidate, BCMA CAR-T (CT053)

- approximately HK$932.5 million (US$119.6 million) (or approximately 31% of the net proceeds) to fund ongoing and planned research and development of our other pipeline product candidates

- approximately HK$601.6 million (US$77.2 million) (or approximately 20% of the net proceeds) for developing full-scale manufacturing and commercialization capabilities

- approximately HK$300.8 million (US$38.6 million) (or approximately 10% of the net proceeds) for continued upgrading of CAR-T technologies and early-stage research and development activities

- approximately HK$270.7 million (US$34.7 million) (or approximately 9% of the net proceeds) will be used for our working capital and other general corporate purposes.

The net proceeds from the Global Offering have been utilized in accordance with the purposes set out in the Prospectus. The table below sets out the applications of the net proceeds and actual usage up to December 31, 2021:

Use of proceeds		**Planned allocation of Net Proceeds** *(HKD million)*	**Planned allocation of Net Proceeds** *(RMB million)*	**Utilized amount (as at December 31, 2021)** *(RMB million)*	**Remaining amount (as at December 31, 2021)** *(RMB million)*
Further development of our Core Product Candidate, BCMA CAR-T (CT053)	30%	902.4	737.8	86.8	651
Ongoing and planned research and development of our other pipeline product candidates	31%	932.5	762.4	143.4	619
Developing full-scale manufacturing and commercialization capabilities	20%	601.6	491.9	138.5	353.4
Upgrading of CAR-T technologies and early-stage research and development activities	10%	300.8	245.9	19.0	226.9
Working capital and other general corporate purposes	9%	270.7	221.3	–	221.3
Total	**100%**	**3,008.0**	**2,459.3**	**387.7**	**2,071.6**

The unutilized amount of net proceeds is expected to be used by 2023.

Saved as disclosed above, we did not have any other issuance of shares for the Relevant Period.

Audit Committee

The Audit Committee has three members comprising Mr. So Tak Young (chairman), Dr. Fan Chunhai and Mr. Guo Huaqing, with terms of reference in compliance with the Listing Rules.

The Audit Committee has considered and reviewed the accounting principles and practices adopted by the Group and has discussed matters in relation to internal controls and financial reporting with the management, including the review of the audited consolidated financial results of the Group for the year ended December 31, 2021. The Audit Committee considers that the financial results for the year ended December 31, 2021 are in compliance with the relevant accounting standards, rules and regulations and appropriate disclosures have been duly made.

Auditor

The figures in respect of the Group's consolidated statement of comprehensive income, consolidated statement of financial position and the related notes thereto for the year ended December 31, 2021 as set out above in this preliminary announcement have been agreed by the Group's auditor, PricewaterhouseCoopers, to the amounts set out in the Group's consolidated financial statements for the year. The work performed by PricewaterhouseCoopers in this respect did not constitute an audit, review or other assurance engagement and consequently no assurance has been expressed by PricewaterhouseCoopers on this announcement.

FINAL DIVIDEND

The Board has resolved not to recommend the payment of a final dividend for the year ended December 31, 2021 (2020: Nil).

ANNUAL GENERAL MEETING

The annual general meeting is scheduled to be held on Wednesday, May 25, 2022 (the "**AGM**"). A notice convening the AGM will be published and dispatched to the shareholders of the Company in the manner required by the Listing Rules in due course.

CLOSURE OF REGISTER OF MEMBERS AND RECORD DATE

The register of members of the Company will be closed from Friday, May 20, 2022 to Wednesday, May 25, 2022, both days inclusive, in order to determine the identity of Shareholders who are entitled to attend and vote at the AGM to be held on Wednesday, May 25, 2022. Shareholders whose name appear on the register of members of the Company on Friday, May 20, 2022 will be entitled to attend and vote at the AGM. In order to be eligible to attend and vote at the AGM, all transfer accompanied by relevant share certificates and transfer forms must be lodged with the Company's share registrar in Hong Kong, Computershare Hong Kong Investor Services Limited, at Shops 1712-1716, 17th Floor, Hopewell Centre, 183 Queen's Road East, Wanchai, Hong Kong before 4:30 p.m. on Thursday, May 19, 2022.

PUBLICATION OF ANNUAL RESULTS ANNOUNCEMENT AND ANNUAL REPORT

This announcement is published on the websites of the Stock Exchange (www.hkexnews.hk) and the Company (www.carsgen.com).

The annual report of the Company for the year ended December 31, 2021 containing all the information required by the Listing Rules will be despatched to the Company's shareholders and published on the websites of the Stock Exchange and the Company in due course.

APPRECIATION

The Board would like to express its sincere gratitude to the shareholders, management team, employees, business partners and customers of the Group for their support and contribution to the Group.

"2019 Equity Incentive Plan"	the equity incentive plan of our Company as adopted by way of written resolutions of the Board on January 22, 2019, the principal terms of which are set out in the section headed "Statutory and General Information — D. 2019 Equity Incentive Plan" in the Prospectus
"affiliate"	any other person, directly or indirectly, controlling or controlled by or under direct or indirect common control with such specified person
"Audit Committee"	the audit committee of the Company
"Board of Directors", "Board" or "our Board"	our board of Directors
"BVI"	the British Virgin Islands
"CARsgen Therapeutics (Shanghai)"	CARsgen Therapeutics Co., Ltd (科濟生物醫藥(上海)有限公司), a company incorporated in the PRC with limited liability on October 30, 2014, and one of our consolidated affiliated entities
"China" or "PRC"	the People's Republic of China, which for the purpose of the Prospectus and for geographical reference only, excludes Hong Kong, Macao and Taiwan
"Company", "our Company", "the Company", "CARsgen Therapeutics" or "CARsgen"	CARsgen Therapeutics Holdings Limited (科濟藥業控股有限公司), an exempted company incorporated in the Cayman Islands with limited liability on February 9, 2018
"Core Product Candidate"	has the meaning ascribed to it in Chapter 18A of the Listing Rules and in this context, refers to CT053
"Corporate Governance Code" or "CG Code"	the Corporate Governance Code set out in Appendix 14 to the Listing Rules
"Director(s)"	the director(s) of the Company
"FDA" or "U.S. FDA" or "US FDA"	U.S. Food and Drug Administration
"Group", "our Group", "we", "us" or "our"	our Company, its subsidiaries and consolidated affiliated entities from time to time or, where the context so requires, in respect of the period prior to our Company becoming the holding company of its present subsidiaries and consolidated affiliated entities, such subsidiaries and consolidated affiliated entities as if they were subsidiaries and consolidated affiliated entities of our Company at the relevant time

"HK$" or "Hong Kong dollars"	Hong Kong dollars, the lawful currency of Hong Kong
"Hong Kong" or "HK"	the Hong Kong Special Administrative Region of the People's Republic of China
"Listing Date"	June 18, 2021
"Listing Rules"	the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited, as amended, supplemented or otherwise modified from time to time
"Model Code"	Model Code for Securities Transactions by Directors of Listed Issuers
"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
"Prospectus"	the prospectus issued by the Company on June 7, 2021 in connection with the IPO
"Relevant Period"	the period from the Listing Date to December 31, 2021
"Reporting Period"	the period from January 1, 2021 to December 31, 2021
"RMB" or "Renminbi"	Renminbi, the lawful currency of China
"Share(s)"	ordinary share(s) in the share capital of our Company with a par value of US$0.00000025 each
"Stock Exchange"	The Stock Exchange of Hong Kong Limited
"United States" or "U.S." or "US"	the United States of America, its territories, its possessions and all areas subject to its jurisdiction
"US$" or "U.S. dollars" or "USD"	United States dollars, the lawful currency of the United States

In this announcement, the terms "associate", "connected transaction", "controlling shareholder" and "subsidiary" shall have the meanings given to such terms in the Listing Rules, unless the context otherwise requires.

"antigen"	the substance that is capable of stimulating an immune response, specifically activating lymphocytes, which are the body's infection-fighting white blood cells
"BCMA"	B-cell maturation antigen, a protein that is highly expressed in several hematologic malignancies
"BLA"	biologics license application
"B2M"	beta 2 microglobulin
"CAR(s)"	chimeric antigen receptor(s)
"CAR-T" or "CAR T"	chimeric antigen receptor T cell
"CD19"	a cell surface protein expressed on the surface of almost all B cell leukemia and lymphoma
"CDC"	complement-dependent cytotoxicity, an effector function of IgG and IgM antibodies
"CDE"	Center for Drug Evaluation, an institution under the NMPA
"CDMO(s)"	contract development manufacturing organization(s), a company that serves other companies in the pharmaceutical industry on a contract basis to provide comprehensive services from drug development through drug manufacturing
"CGMP"	Current Good Manufacturing Practice
"chemotherapy"	a category of cancer treatment that uses one or more anti-cancer chemotherapeutic agents as part of its standardized regimen
"CLDN18.2"	Claudin18.2, an attractive target in the treatment of certain solid tumors such as gastric cancer, esophageal cancer and pancreatic cancer
"CMC"	chemistry, manufacturing and controls processes in the development, licensure, manufacturing and ongoing marketing of pharmaceutical products
"cohort"	a group of patients as part of a clinical study who share a common characteristic or experience within a defined period and who are monitored over time

"combination therapy"	treatment in which a patient is given two or more therapeutic agents for a single disease
"CR"	complete response, the disappearance of all signs of cancer in response to treatment
"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
"CTA"	Clinical Trial Application
"CycloCAR®"	a next-generation CAR-T technology under development by the Company, which features co-expression of cytokines IL-7 and chemokine CCL21 in the CAR T cells to potentially improve clinical efficacy and reduced requirement for lymphodepletion conditioning
"cytokine"	a broad and loose category of small proteins that are important in cell signaling. Their release has an effect on the behavior of cells around them
"cytotoxic"	toxic to living cells
"DOR"	duration of response
"EGFR"	epidermal growth factor receptor
"EGFRvIII"	variant III of epidermal growth factor receptor
"EMA"	European Medicines Agency
"GPC3"	Glypican-3, an oncofetal antigen expressed in a variety of tumors including certain liver and lung cancers
"Grade"	term used to refer to the severity of adverse events
"GvHD"	graft versus host disease
"HCC"	hepatocellular carcinoma, a type of cancer arising from hepatocytes in predominantly cirrhotic liver
"Health Canada"	the department of Canada's government with responsibility for national public health

"HLA"	human leukocyte antigen
"HvGR"	host versus graft response
"IIT" or "investigator-initiated trial"	clinical trial sponsored and conducted by independent investigators
"IND"	investigational new drug or investigational new drug application, also known as clinical trial application in China
"LADAR®"	Local Action Driven by Artificial Receptor technology, with similar mechanism of synNotch system, in which the intracellular transcription of the gene of interest is controlled by a chimeric regulatory antigen receptor
"mAb" or "monoclonal antibody"	antibodies that are made by identical immune cells which are all clones belonging to a unique parent cell
"mesothelin"	cell-surface protein whose expression is mostly restricted to mesothelial cell layers lining the pleura, pericardium and peritoneum
"MM" or "R/R MM"	multiple myeloma, a type of cancer that forms in the white blood cells; cancer that relapses or does not respond to treatment is called relapsed and/or refractory multiple myeloma
"NDA"	new drug application
"NHL"	non-Hodgkin's lymphoma
"NK cell"	natural killer cell, the human body's first line of defense due to their innate ability to rapidly seek and destroy abnormal cells
"NKG2A"	also named KLRC1, killer cell lectin-like receptor subfamily C, member 1
"neurotoxicity"	possible adverse side effect of T cell therapies that leads to a state of confusion, aphasia, encephalopathy, tremor, muscular weakness, and somnolence
"ORR"	objective response rate
"OS"	overall survival

"Phase I"	a study in which a drug is introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage, tolerance, absorption, metabolism, distribution, excretion, and if possible, to gain an early indication of its effectiveness
"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"	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
"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
"PR"	partial response
"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 medicine's benefits and risks, and accelerate assessment of medicines applications, for medicines that target an unmet medical need with advantages over existing treatments
"progressive-free survival" or "PFS"	the length of time during and after the treatment of a disease, such as cancer, that a patient lives without tumor progression or death
"regenerative medicine advanced therapy" or "RMAT"	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
"registrational trial"	large confirmatory studies meant to establish an acceptable benefit/safety profile in order to gain regulatory approval for a precisely defined indication
"RTP"	Research Triangle Park
"solid tumor"	an abnormal mass of tissue that usually does not contain cysts or liquid areas

"TCR"	T cell receptor
"TCR$^-$/HLA$^-$"	the deficiency of T cell receptor and human leukocyte antigen
"THANK-uCAR®"	the Company's proprietary technology to generate CAR T cells with improved expansion and persistence from T cells that are sourced from third-party donors
"TKI"	tyrosine kinase inhibitor, a pharmaceutical drug that inhibits tyrosine kinases

For the purpose of this announcement and for illustration purpose only, conversion of HK$ to RMB is based on the exchange rate of HK$1 to RMB0.8176.

By Order of the Board
CARsgen Therapeutics Holdings Limited
Dr. Li Zonghai
Chairman

Hong Kong, March 22, 2022

As at the date of this announcement, the board of directors of the Company comprises Dr. Li Zonghai and Dr. Wang Huamao as executive Directors; Mr. Guo Bingsen, Mr. Guo Huaqing, Mr. Xie Ronggang and Ms. Zhao Yachao as non-executive Directors; Dr. Fan Chunhai, Dr. Yan Guangmei and Mr. So Tak Young as the independent non-executive Directors.