OVERVIEW

We are a leading clinical-stage biopharmaceutical company in China with a fully-integrated proprietary biologics platform in bispecifics and protein engineering. Our mission is to deliver world-class innovative therapeutic biologics to treat patients globally by applying our unique drug discovery and development capabilities. We believe our unique drug discovery and development capabilities are demonstrated by our strong R&D track record and supported by our proprietary technologies, platforms and expertise.

Our highly differentiated in-house pipeline includes:

- *KN046* – a BsAb immune checkpoint inhibitor simultaneously targeting two clinically-validated immune checkpoints, PD-L1 and CTLA-4, representing a potential breakthrough, next-generation immuno-oncology blockbuster drug. As of the Data Cut-off Date, in our phase I clinical trials in Australia and China, among all evaluable subjects receiving KN046 at 5.0 mg/kg Q2W (RP2D), the DCR was 77.8% and 69.2%, respectively, and 10 (55.6%) and 4 (30.8%) subjects had target lesion shrinkage, respectively. These subjects have generally failed at least first-line standard of care. The results from the phase I clinical trials have shown a favorable safety profile, and early efficacy signals on NPC (especially in subjects with high PD-L1 expression), and gastrointestinal cancers (including pancreatic cancer). We have adopted a fast/first-to-market approach on select indications and we plan to submit the first BLA for KN046 in China for third or later-line unresectable/metastatic NPC in 2021. We are also conducting clinical trials for several major cancer indications, including NSCLC, TNBC and ESCC. As of the Data Cut-off Date, in our phase II clinical trial in China for second-line or later-line NSCLC subjects (all failed first-line chemotherapy), the DCR was 85.7% and the ORR was 28.6%. As of the same date, in the phase II clinical trial of KN046 as a first-line therapy combined with chemotherapy for first-line TNBC subjects in China, all three evaluable subjects achieved disease control and the ORR was 66.7%. Such preliminary results indicate promising efficacy of KN046 for these two indications especially the combination therapy with chemotherapy.

- *KN026* – a next-generation anti-HER2 BsAb that can simultaneously bind two distinct clinically-validated epitopes of HER2, resulting in potentially superior efficacy. As of September 20, 2019, in our China phase I clinical trial of KN026, KN026 had shown early efficacy signals on heavily pre-treated breast cancer patients as well as a favorable safety profile. In this trial, the overall DCR and ORR was 71.4% and 28.6%, respectively, and a total of 19 (90.5%) evaluable subjects had target lesion shrinkage. Among all the evaluable subjects receiving KN026 at 20.0 mg/kg Q2W or 30.0 mg/kg Q3W (RP2Ds), the DCR was 80.0%, the ORR was 40.0%, and 93.3% subjects had target lesion shrinkage. We plan to complete the phase Ib trial for HER2 High breast cancer and GC/GEJ in China by the first half of 2020. We are also conducting a phase II clinical trial for HER2-overexpressing GC/GEJ in China and a phase I clinical trial for HER2-overexpressing solid tumors, including but not limited to breast cancer and GC/GEJ, in the United States.

- *KN019* – a CTLA-4-based immunosuppressant fusion protein with a clinically-validated mechanism of action and potential broad applications in both autoimmune diseases and oncology treatment-induced immune disorders. We plan to start a phase II trial for RA in the fourth quarter of 2019 and expand to oncology treatment-induced immune disorder indications in the future.

- *KN035* – potentially the first subcutaneously injectable PD-L1 inhibitor worldwide, offering advantages in safety, convenience, compliance, access to patients not suitable for intravenous infusion, and lower medical cost. Invented by us and jointly developed with 3DMed, KN035 is currently undergoing a phase II pivotal clinical trial for dMMR/MSI-H solid tumors and a phase III pivotal trial for BTC in China. The first BLA for KN035 is expected to be filed by the end of 2020 for dMMR/MSI-H solid tumors.

We have a strong research and development team led by our Founder Dr. Xu, a prolific scientist who has made contributions to over 100 patents and patent applications since 2011. As of the Latest Practicable Date, our team had contributed to the CMC processes of many biosimilar candidates. Four of these candidates filed BLAs since 2017, out of a total of 11 biosimilar BLAs that had been filed in China during this period. Our team had also authored 14 papers published in high-impact journals, including *Cancer Cell* and *Immunity.* As of the Latest Practicable Date, we owned one patent covering KN026 in China, co-owned one patent with 3DMed covering KN035 in Australia, and co-owned five patents with Suzhou Alphamab covering our CRIB and CRAM platforms, including in China and the United States. As of the same date, we owned or co-owned 23 patent applications worldwide relating to our drug candidates and technology platforms.

The depth and breadth of our in-house R&D and manufacturing capabilities are demonstrated by the following: (i) structure-guided protein engineering capability to develop protein building blocks in various formats, including sdAbs and engineered proteins; (ii) proprietary CRIB and CRAM platforms for bispecifics and antibody mixtures, respectively; and (iii) state-of-the-art manufacturing capability to be further strengthened by new facilities with an expected capacity of over 30,000L, designed and built to meet NMPA and EU/FDA's cGMP standards.

COMPETITIVE STRENGTHS

Next-generation in-house developed bispecific antibody candidates with blockbuster potential

We are developing a number of next-generation bispecific antibody drug candidates in clinical and pre-clinical stages.

KN046 – BsAb immune checkpoint inhibitor

Our KN046, a BsAb immune checkpoint inhibitor, is potentially a breakthrough, next-generation immuno-oncology blockbuster drug. In 2018, global sales of immune checkpoint inhibitors reached US$20.7 billion. To date, all of the immune checkpoint inhibitors on the market are monospecific antibodies against PD-1, PD-L1 or CTLA-4, which have become successful treatments, including the standard of care for various cancer indications, according to the CIC Report. However, many cancer patients have limited responses to a

single-agent blockade of PD-(L)1 or CTLA-4. To date, one anti-PD-1/CTLA-4 combination therapy has been approved in melanoma, renal cancer carcinoma and colorectal cancer, with significant efficacy improvements in response rate and durability compared to monotherapies of single agents, according to the same source. However, increased toxicity was also observed in this combination therapy due to over-activation of the immune system by the dual blockade. In the registration trials of the combination therapy for melanoma, renal cancer carcinoma and colorectal cancer, much higher treatment-related TEAE rates were reported compared with monotherapies of single agents. Such toxicity profile indicates safety concerns and in turn leads to a narrow therapeutic window. For the combination therapy, the highest approved dosage for each agent is 3.0 mg/kg (up to 12 weeks of concurrent usage).

Our KN046 is potentially the first global BsAb that simultaneously targets two clinically-validated immune checkpoints, PD-L1 and CTLA-4. To reduce toxicity of the dual blockade, we engineered our KN046 with targeted drug delivery that directs it primarily to tumor-related micro-environments. KN046 has exhibited a favorable safety profile based on available results of our phase I clinical trials. As of the Data Cut-off Date, in the phase I clinical trials in Australia and China, treatment-related TEAEs at grade 3 or higher levels were reported in 20.7% (95% CI, 8.0% to 39.7%) and 4.5% (95% CI, 0.1% to 22.8%) of the enrolled subjects receiving KN046 at 5.0 mg/kg Q2W (RP2D), respectively. As of the same date, in the phase I clinical trial in Australia, 29 (54.7%) subjects received KN046 at the RP2D, and out of all 23 subjects with a treatment duration of at least 12 weeks in this trial, one subject discontinued treatment due to treatment-related TEAEs. As of the same date, in the phase I clinical trial in China, 22 (33.9%) subjects received KN046 at the RP2D, and out of all 26 subjects with a treatment duration of at least 12 weeks in this trial, none discontinued treatment due to treatment-related TEAEs. These preliminary results indicate a broader therapeutic window. We believe that a broad therapeutic window can contribute to increased efficacy associated with higher and longer drug exposure. As of the Data Cut-off Date, among all evaluable subjects receiving KN046 at 5.0 mg/kg Q2W (RP2D) in the phase I clinical trials in Australia and China, the DCR was 77.8% and 69.2%, respectively, and 10 (55.6%) and 4 (30.8%) subjects had target lesion shrinkage, respectively. These subjects have generally failed at least first-line standard of care. The results from the phase I clinical trials have shown a favorable safety profile, and early efficacy signals on NPC (especially in subjects with high PD-L1 expression), and gastrointestinal cancers (including pancreatic cancer). As of the Data Cut-off Date, in our phase II clinical trial in China for second-line or later-line NSCLC subjects (all failed first-line chemotherapy), the DCR was 85.7% and the ORR was 28.6%. As of the same date, in the phase II clinical trial of KN046 as a first-line therapy combined with chemotherapy for first-line TNBC subjects in China, all three evaluable subjects achieved disease control and the ORR was 66.7%. Such preliminary results indicate promising efficacy of KN046 for these two indications especially the combination therapy with chemotherapy.

With a favorable safety profile and potentially superior efficacy over existing immune checkpoint inhibitors, we believe that our KN046 has blockbuster potential. We received an Umbrella IND approval from the NMPA for KN046 in July 2018. We had completed phase Ia dose escalation studies and were currently conducting the phase Ib dose expansion studies in Australia and China. As of the Latest Practicable Date, we were conducting four phase II clinical trials for NSCLC, TNBC and ESCC in China.

KN026 – BsAb anti-HER2 antibody

KN026, a BsAb anti-HER2 antibody, is potentially a global next-generation HER2-targeted therapy. To date, the two most widely prescribed anti-HER2 mAbs on the market (i.e., trastuzumab and pertuzumab), are monospecific antibodies, according to the CIC Report. In 2018, the aggregate global sales of these drugs reached US$9.9 billion, of which trastuzumab accounted for 71.6%, according to the same source. The advent of these antibody drugs significantly improved the treatment efficacy in patients with HER2 High breast cancer and GC/GEJ. However, a number of other major HER2 High cancer indications, such as certain subtypes of GI cancers, urothelial cancer and ovarian cancer, are not covered by current anti-HER2 antibody therapies, which represents a significant unmet medical need. In addition, there are a substantial number of patients with breast cancer, GC/GEJ or other types of cancers that express HER2 at low to intermediate levels, which are also ineligible for current anti-HER2 antibody therapies.

We expect our KN026 to be able to address these unmet medical needs with superior efficacy and broader indication coverage. KN026 is a BsAb that can simultaneously bind two distinct clinically-validated epitopes of HER2, resulting in (i) a dual blockade of HER2-related signaling pathways, (ii) strengthened binding to HER2 receptors, (iii) a reduction of HER2 proteins on the cell surface, and (iv) increased tumor killing effect. These combined mechanisms of action can potentially enable KN026 to have a superior tumor inhibition effect. As of September 20, 2019, in our China phase I clinical trial of KN026, the overall DCR and ORR was 71.4% and 28.6% respectively, and a total of 19 (90.5%) of the evaluable subjects had target lesion shrinkage. Among all the evaluable subjects receiving KN026 at 20.0 mg/kg Q2W or 30.0 mg/kg Q3W (RP2Ds), the DCR was 80.0%, the ORR was 40.0% and 93.3% subjects had target lesion shrinkage. Our KN026 has shown efficacy for patients with HER2 High breast cancer after numerous prior treatments, including trastuzumab, targeted small molecule drugs and an investigational ADC drug candidate. In pre-clinical studies, KN026 has shown better tumor inhibition effect than the combination of trastuzumab and pertuzumab against different HER2 High cancer cell lines. KN026 also exhibited tumor inhibition activities for a HER2 Low cancer cell line.

We received an Umbrella IND approval from the NMPA and an IND approval from the FDA in March 2018 and October 2018, respectively. We are currently conducting a phase I clinical trial of KN026 in China for HER2 High breast cancer and GC/GEJ, and the preliminary results have shown a favorable safety profile and early efficacy signals. We are also conducting a phase II clinical trial for HER2-overexpressing GC/GEJ in China and a phase I clinical trial for HER2-overexpressing solid tumors, including but not limited to breast cancer and GC/GEJ, in the United States.

Pre-clinical drug candidates

We have four pre-clinical bispecific candidates targeting various pathways for tumor microenvironment modulations. We are in the process of concluding pre-clinical studies and plan to file IND for one or two candidates within the next two years.

Robust pipeline of other in-house developed candidates

In addition to KN046 and KN026, we have two drug candidates with significant commercial potential.

KN019 – CTLA-4-based immunosuppressant fusion protein

We are developing KN019, a CTLA-4-based immunosuppressant fusion protein drug candidate. KN019 functions at the early stage of T-cell activation and therefore may lead to efficient global downregulation of unwanted immune responses. Oncology treatments may induce immune disorders, such as severe irAEs, GvHD and CRS, which can become life-threatening if not managed properly. KN019 has the potential to become a treatment option for these conditions and a supportive therapy to oncology treatment. CIC estimates that approximately 100,000 patients in China are suffering from the aforementioned immune disorders without effective treatment, indicating an attractive market with significant unmet needs.

There is no CTLA-4-Fc fusion protein approved in China. Globally, the immunosuppression effect of CTLA-4-Fc fusion proteins have been proven by Nulojix (belatacept) and Orencia (abatacept). Orencia is approved for RA, idiopathic arthritis and psoriatic arthritis with global sales of US$2.7 billion in 2018. Nulojix is an improved version of Orencia with higher potency and is approved for post-transplant kidney rejection. Considering that these indications are approved indications, and our KN019 has the same amino acid sequence as belatacept, we are focusing on RA and post-transplant kidney rejection as indications for near-term clinical development, which we expect will accelerate the registration process of KN019 and generate a potential near-future commercial benefit. This near-term focus also enables us to validate our fusion protein molecules first to facilitate expansion to potential applications in oncology treatment-induced immune disorders, such as severe irAEs, GvHD and CRS.

KN035 – subcutaneous PD-L1 inhibitor with near-term commercialization potential

We invented KN035 in-house and currently are jointly developing it with 3DMed. KN035 is potentially the first subcutaneously injectable PD-L1 inhibitor worldwide. To date, all approved PD-(L)1 inhibitors are intravenously administered, which requires frequent infusion services, increases the risk of infusion-related reactions, and may not be used in patients with limited vein access. Compared to intravenous administration, subcutaneous injections offer advantages in safety, convenience, compliance, access to patients not suitable for intravenous infusion, and lower medical cost. The success of subcutaneous formulations has been demonstrated by multiple drug products. For example, the 2013 launch of the Herceptin subcutaneous formulation in Europe captured a 50% share of the European market in only four years after launch, according to the CIC Report. We believe that our KN035 has vast potential in the PD-(L)1 inhibition market in China, which is expected to be US$10.4 billion by 2030, according to the CIC Report.

Under our partnership with 3DMed, we own the right to manufacture and supply KN035 to 3DMed and are entitled to share the profits generated from KN035's global sales after its commercialization. As of the Latest Practicable Date, KN035 was undergoing late-stage clinical development. We believe that our KN035 partnership enables us to benefit from the sales of a potential blockbuster drug in the near term without making large investments.

Fully-integrated platform supporting drug discovery, development and manufacturing

We have built a fully-integrated biologics platform covering the entire process for drug discovery and development, which we believe will allow us to discover, develop and manufacture a robust and commercially-viable product pipeline with the following key advantages:

- *Research capabilities in discovery and clinical development.* Our in-house research and development team, led by Dr. Xu, possesses in-depth expertise on structure-guided protein engineering which enables us to develop protein building blocks in various formats, including conventional monoclonal antibodies, sdAbs, bispecific antibodies and engineered proteins. Leveraging our proprietary CRIB and CRAM platforms, we are able to design and evaluate multiple combinations of these building blocks and select the optimal candidates early in development. As a result, we have successfully developed four clinical-stage candidates with a wide range of biologics formats, being our bispecific KN026, sdAb-based KN046 and KN035, and fusion protein-based KN019. Our robust in-house clinical development team enables us to lead and control the clinical trial process under a more adaptive design with signal-driven processes, which enables a rapid response during clinical studies to achieve flexibility in indication selection and maximize efficiency in clinical development.

- *Process development expertise.* Our process development capabilities have been demonstrated by our clinical assets, including a heterodimeric antibody, and novel and/or complex fusion proteins such as our KN019, KN046 and KN035. The consistency of their CMC processes have been validated by multiple batches of large-scale production. As of the Latest Practicable Date, we owned one patent covering KN026 in China, co-owned one patent with 3DMed covering KN035 in Australia, and co-owned five patents with Suzhou Alphamab covering our CRIB and CRAM platforms.

- *Manufacturing capabilities.* We currently supply clinical development with 2x1,000L production lines designed and constructed to meet the NMPA and FDA's applicable regulatory requirements and GMP standards. We have advanced manufacturing facilities under construction with an expected capacity of over 30,000L. Phase I of these facilities, with a 4,000L (2x2,000L) production capacity, is expected to be completed in late 2019. Our new manufacturing facilities are designed to meet NMPA and EU/FDA's cGMP requirements, supported by our comprehensive in-house quality management system. We have equipped our large-scale production with advanced technology platforms, CMC processes and know-how. For example, our CRAM platform enables us to produce multiple antibodies in one stable cell line, which enables us to reduce cost and time consumed compared to separate antibody manufacturing processes.

Visionary founder supported by an experienced management team

Our founder, Dr. Xu, built our company with the goal of developing world-class, innovative therapeutic biologics for cancer patients globally. Prior to founding our Group, Dr. Xu served as senior scientist and investigator at a number of multinational biopharmaceutical companies, including EMD Serono Research Institute Inc. (now part of Merck KGaA) and

Biogen IDEC Inc. He has also made contributions to over 100 patents and patent applications since 2011. Under the leadership of Dr. Xu, as of the Latest Practicable Date, our R&D team had contributed to the CMC processes of many biosimilar candidates. Four of these candidates filed BLAs since 2017, out of a total of 11 biosimilar BLAs that have been filed in China during this period.

In 2018, in light of his achievements, Dr. Xu was recognized as one of the Top 10 Talent for Innovation and Entrepreneurship in Jiangsu in 2018. Dr. Xu has been engaged in the frontier research of oncology, immunology and protein chemistry for many years with 14 research papers in high-impact journals. Currently, Dr. Xu also serves as an adjunct professor at Shanghai Institute of Materia Medica, Chinese Academy of Sciences (中國科學院上海藥物研究所), and School of Life Sciences and Biotechnology of Southeast University (東南大學生命科學與技術學院) in China, enabling him to keep abreast of the latest academic research and industry development trends.

Dr. Xu is supported by a senior management team with a wide range of complementary skill sets covering research, clinical development and manufacturing in the biopharmaceutical industry. Our senior management team has extensive industry experiences at domestic and international biotech companies, and has contributed to research and development of a number of blockbuster oncology drugs, such as Merck's Keytruda (pembrolizumab) and Roche's Herceptin (trastuzumab).

BUSINESS STRATEGY

Rapidly advance clinical development of our product pipeline

We plan to advance the following clinical development plans for our product pipeline:

- *KN046*. We plan to develop our KN046, which simultaneously targets both PD-L1 and CTLA-4, for various cancer indications. Based on available clinical results and our analysis of the competitive landscape and patient population, we are executing the following clinical development plan:

  - *Fast/First-to-market strategy*. Under a fast/first-to-market approach, we initiated a dose expansion phase of the phase I clinical trial in China in July 2019 with a strategic focus on late-line unresectable/metastatic NPC, urothelial cancer and melanoma using KN046 as a monotherapy. Patients with these late-line indications have limited choices of existing therapies, which allows us to conduct single arm registration trial(s) with a much smaller patient size compared to major indications. We plan to advance the trial for NPC first, considering the early efficacy signals observed in the phase I clinical trial in China. We expect to file the first BLA for KN046 with the NMPA in 2021 for this indication.

  - *Major indications*. To explore the vast market potential of immune checkpoint inhibitors, we plan to strategically develop KN046 for several major cancer indications, including but not limited to NSCLC, TNBC and ESCC. We are

conducting two phase II clinical trials for non-EGFR and non-ALK mutant locally advanced unresectable or metastatic NSCLC, including one for PD-(L)1 refractory cancer patients. We are also conducting a phase Ib/II clinical trial for locally advanced or metastatic TNBC and a phase II clinical trial for locally advanced/recurrent or metastatic ESCC. Considering the preliminary promising efficacy results observed on NSCLC and TNBC subjects, we may initiate phase III trials and expand these trials to the United States as global trials, subject to receiving IND approval from the FDA.

- *Combination therapy*. As a potential next-generation immuno-oncology cornerstone drug, we believe KN046 has significant potential to be combined with other cancer therapies, such as chemotherapy, targeted small molecule drugs, multiple-TKI drugs and other immune checkpoint inhibitors. Such combinations may enhance efficacy, overcome resistance and minimize side effects. Within our own product pipeline, we plan to conduct a basket trial for four late-stage HER2 High cancers in combination with our KN026 to improve response rates and maximize the market value of our pipeline products, see "—KN026" below.

- *Indications with unmet medical needs*. We are actively seeking indications with unmet medical needs, such as anti-PD-(L)1 refractory cancers, and soft tissue sarcoma. We plan to initiate a pivotal trial in China for specific subtypes of locally advanced unresectable or metastatic soft tissue sarcoma, considering the significant patient population and the fact that there are only a few on-going clinical trials globally for this indication. If the preliminary results are positive, we plan to expand this trial to the United States and form a global trial, subject to receiving IND approval from the FDA.

- *KN026.* As HER2 High cancers are expected to be most responsive to anti-HER2 antibody drugs, we plan to strategically focus on HER2 High cancers in our KN026 clinical development plan. We plan to initiate a pivotal phase III clinical trial for HER2 High metastatic breast cancer in the second quarter of 2020 to investigate KN026 as a first-line treatment in combination with chemotherapy. Depending on clinical data from the KN026-CHN-001 trial and KN026-US-001 trial, we may consider initiating a pivotal trial for the third-line or later-line treatments of breast cancer. In addition to breast cancer, there are a number of other cancer types closely associated with HER2 overexpression and untapped by current anti-HER2 antibody drugs. We plan to conduct a phase II basket trial in China for HER2 High gastric cancer and other gastrointestinal cancers, urothelial cancer and ovarian cancer with the combination therapy of KN026/KN046. Studies have suggested that the trastuzumab and pertuzumab combination therapy reached an ORR of 33.3% in urothelial cancer patients. Therefore we believe that the KN026/KN046 combination can potentially offer superior ORR and DOR, which may translate into a further improved overall survival benefit and enable a chemotherapy-free first-line therapy for urothelial cancer. If promising efficacy signals were observed in a majority of the selected indications, we plan to expand the basket trial into a pivotal trial.

Advance our pre-clinical and discovery programs

Leveraging our strong in-house R&D capabilities, we plan to further advance our pre-clinical programs of four bispecific immune-oncology drug candidates. We are in the process of concluding pre-clinical studies and plan to file IND for one or two candidates within the next two years. Moreover, with a focus on immuno-oncology-based bispecific and multi-specific drugs, we plan to leverage our technology platforms to discover, validate and select targets and lead compounds to enrich our early-stage pipeline.

Continue to enhance our manufacturing capabilities

We plan to continue to optimize our manufacturing process and technologies to enhance product quality and control costs. In particular, we are developing our in-house cell culture media, which we believe will ensure quality and timely supplies that match our specific production requirements in a cost effective manner. In addition, we are exploring CMC development for different drug formulations to improve patient experience and convenience when administering our drugs. We also plan to further develop our culture expansion processes as we prepare to transfer and scale-up manufacturing at our new facilities.

We intend to gradually transfer our manufacturing activities from the facility we currently lease to our own facilities, and transfer the processes previously outsourced to CMOs in China to in-house. In the United States, we plan to continue to work with industry-leading and reputable CMOs to improve cost efficiency and lower our regulatory compliance costs.

Continue to attract, train and retain talent to further expand our capabilities

To support our continued growth, we aim to build a talent pool and enhance our capabilities in various aspects of our operations including finance, business development, manufacturing, legal and general administrative support, in particular, research, clinical development and commercialization.

Our robust oncology pipeline is built on our exceptional expertise in the discovery and development of immuno-oncology drugs. To strengthen our competitive advantages, we plan to continue to enhance the capabilities and capacity of our clinical development team and gradually expand geographically outside China, to advance the pivotal trials and support regulatory approvals in our target markets.

In line with the clinical trial advancement of our drug candidates, we intend to develop a road map for product commercialization in China. We aim to build a highly specialized and efficient oncology commercial team to drive product launch and bring innovative cancer therapies to our target markets. We plan to assemble a core commercial leadership team with extensive experience in the pharmaceutical industry and to establish a commercialization team with approximately 100 members in 2021. We are also evaluating options for commercial partnership to accelerate commercial ramp up and maximize market potential of our assets in the U.S. market.

Seek value-maximizing collaboration opportunities

We actively seek strategic collaboration opportunities to maximize the commercial value of our assets with global rights. We have adopted a hybrid strategy to develop combination therapies, including in-house development of combination therapies of KN046 and KN026, and collaborations with third parties to target the opportunities in the growing combination therapy market. We plan to select candidates for combination therapies by considering a number of factors, including scientific rationales for efficacy improvement, safety profile and tolerability of the proposed combination, potential market opportunities, competing drugs and cost for combination development. To date, we have entered into a collaboration agreement with Sunshine Lake to co-develop a combination therapy of our KN046 and their CT-053 (an anti-tumor small molecule drug candidate at clinical stage), for the treatment of HCC. See "—Our Collaboration Arrangements." In the United States and other regions, we are actively exploring collaboration opportunities by closely monitoring industry developments and the competitive landscape and selecting strategic partners with strong synergies to maximize the value of our drug candidates.

OUR PRODUCT PIPELINE

Overview

As of the Latest Practicable Date, we had a total of eight oncology drug candidates in our product pipeline, four of which were in clinical stage. The following table summarizes our product pipeline.

Drug candidate	Target(s)	Main indications[1]	Therapeutic biologic product classification	Commercial rights	Status**					Expected first BLA submission
					Pre-clinical[2]	Dose escalation Phase Ia/I	Dose expansion phase Ib/II	Pivotal Phase II/III	NCT Number	
KN046*	PD-L1/ CTLA4	Solid tumors[3], NSCLC, TNBC, GI cancers including pancreatic cancer	Category 1	Global[4]	China (the NMPA)[6][7]		Phase Ib/II		NCT03838848 NCT03872791 NCT03925870 NCT04054531	3Q 2021
					Australia (the TGA)[8]		Phase Ib		NCT03529526	
KN026	HER2/ HER2	HER2-overexpressing mBC and GC/GEJ	Category 1	Global[4]	China (the NMPA)[6]		Phase II		NCT03925974	4Q 2022
					U.S. (the FDA)[9]	Phase I			NCT03847168	
KN019	B7	RA, post-transplant kidney rejection	Category 7	Global[4]	China (the NMPA)[6]		Phase II (initiation preparation)		NCT04038970	Planning stage
KN035	PD-L1	BTC, MSI-H or dMMR solid tumors, HCC, GC	Category 1	Co-development[5]	China (the NMPA)[6]			Phase II/III	NCT03478488 NCT03667170	By the end of 2020
					Rest of the world[10]				NCT02827968 NCT03248843	
KN052	Undisclosed bispecifics[11]			Global					Not available	Not available
KN053				Global						
KN055				Global						
KN058				Global						

Abbreviations: NSCLC = non-small cell lung cancer, TNBC = triple-negative breast cancer, mBC=metastatic breast cancer, GC = gastric cancer, GEJ = gastroesophageal junction cancer, HCC = hepatocellular carcinoma, BTC = biliary tract cancer, RA = rheumatoid arthritis, MSI-H = high microsatellite instability, dMMR = DNA mismatch repair, GI cancer = gastrointestinal cancer.

* Denotes Core Product.

** Denotes the most advanced ongoing clinical trials.

(1) We also plan to develop (i) KN046 for esophageal squamous cell carcinoma; and (ii) KN026 for gastric cancers and other types of gastrointestinal cancers, urothelial cancer and ovarian cancer in combination with KN046.

(2) Among the four pre-clinical bispecific candidates, two are at preliminary pre-clinical study stage and two at lead-optimized stage.

(3) The phase Ib study of KN046 targeted various types of solid tumors, with a focus on late-line unresectable metastatic nasopharyngeal carcinoma, urothelial cancer and melanoma. It should be noted that these indications are not major cancer indications in China, each with a relatively low cancer incidence and representing a small fraction of the total cancer population in China, according to the CIC Report. See "Industry Overview—Overview of Oncology Drug Market in the PRC and United States." We plan to submit the first BLA for KN046 in China for NPC in 2021.

(4) No licensing partner/collaborator as of the Latest Practicable Date.

(5) We invented KN035 in-house and currently are jointly developing it with 3DMed for clinical trials. According to the Co-development Agreements, upon receiving the BLA approval for KN035, 3DMed would be

responsible for its global commercialization. We own the right to manufacture and supply KN035 to 3DMed and are entitled to profit sharing. See "—Our Collaboration Arrangements—Co-development Agreements with 3DMed."

(6) All of our clinical-stage drug candidates received Umbrella IND approvals from the NMPA. Some indication(s) may not require a non-pivotal phase II clinical trial prior to beginning the pivotal phase II/III clinical trials in China. Based on our experience, the need for comparison studies for our drug candidates is considered on a case-by-case basis and based on communications with the NMPA.

(7) We conducted the China phase Ia clinical trial as a bridging study to leverage our clinical trial data in Australia.

(8) Except for the phase I clinical trial, we do not expect to conduct any other clinical trials or make any registration filing for KN046 in Australia.

(9) KN026 received the IND approval from the FDA in October 2018. We could use clinical trial data in China to support clinical trials in the U.S. or initiate pivotal II/III clinical trials for some indication(s) without conducting non-pivotal phase II clinical trials in the U.S.

(10) Phase I clinical trials are ongoing in the United States and Japan. KN035 received the IND approvals from the U.S. FDA and the Japan Pharmaceuticals and Medical Devices Agency in November 2016 and May 2017, respectively. 3DMed is responsible for clinical trials and registration filings under the Co-development Agreements.

(11) Due to commercial sensitivity, we do not disclose additional details of these BsAb drug candidates for oncology treatment.

Anti-PD-L1/CTLA-4 BsAb Candidate – KN046

Overview

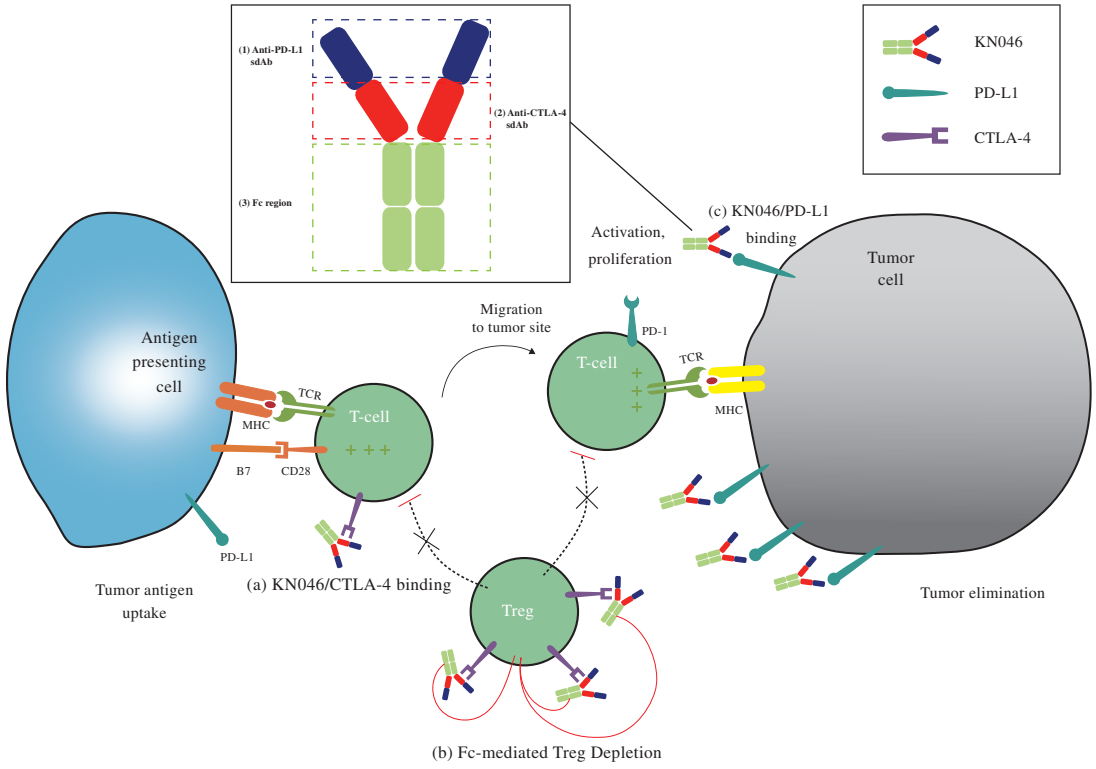
Our KN046 is potentially the first global BsAb that simultaneously targets two clinically-validated immune checkpoints, PD-L1 and CTLA-4. To date, all of the immune checkpoint inhibitors on the market against CTLA-4 and PD-(L)1 are monospecific antibodies. However, many cancer patients have limited responses to PD-(L)1 or CTLA-4 inhibitors alone. An anti-PD-1/CTLA-4 combination therapy has been approved with higher efficacy in certain indications. However, the combination therapy has safety concerns and a narrow therapeutic window. As a dual blockade therapy, KN046 potentially has efficacy advantages over single-agent immune checkpoint inhibitors. Compared with the approved combination therapy, KN046 potentially has a favorable safety profile and a broad therapeutic window, which may allow for a higher dose level and longer drug exposure.

In July 2018, we received an Umbrella IND approval from the NMPA for the initiation of clinical trials for KN046. KN046 is the only anti-PD-(L)1/CTLA-4 candidate entering phase II clinical trials. We are executing a comprehensive clinical trial development plan in China, Australia and the United States targeting an array of cancer indications either as a monotherapy or in combination with other therapies, with the purpose of supporting registration of KN046 for multiple indications in China and the United States. We had completed phase Ia dose escalation studies and were currently conducting the phase Ib dose expansion studies in Australia and China. We completed subject enrollment for the phase I clinical trial in Australia in October 2019. We are also conducting a number of ongoing phase II clinical trials for multiple indications.

Mechanism of Action

Our KN046 is a BsAb candidate that simultaneously targets two different immune checkpoints, PD-L1 and CTLA-4. CTLA-4 functions on activated T-cells primarily in lymph nodes during the early priming phase of immune responses. During the priming phase, T-cells become activated if their T-cell receptors recognize and bind to antigens on MHC complexes and their CD28 co-stimulatory receptors bind to B7 ligands on antigen presenting cells.

CTLA-4 has a higher affinity for B7 ligands and outcompetes CD28 for binding B7 ligands, and CTLA-4/B7 binding has an inhibitory effect on T-cell activation. PD-L1, a ligand of PD-1, interacts with PD-1 to suppress activated T-cells later in the effector phase. During the effector phase, activated T-cells migrate to the tumor site to kill malignant cells. Tumors or bystander antigen presenting cells may, however, upregulate PD-L1 and obstruct T-cell function by inducing inhibitory intracellular signaling. Additionally, constitutive over-expression of CTLA-4 on tumor resident Tregs is important to suppressive functions on T-cells. By taking advantage of the differences of PD-L1 and CTLA-4 in terms of the timing of downregulation and the responsible signaling mechanisms, we believe our KN046 can augment T-cell activation and proliferation, restore T-cell immune responses and reduce Treg-mediated immunosuppression in tumor-related micro-environment. This leads to a potential synergistic effect that should result in a stronger and longer lasting anti-tumor response. The following diagram illustrates the mechanism of action of our KN046.



(a) CTLA-4/B7 binding has an inhibitory effect on T-cell activation. Binding of the anti-CTLA-4 sdAb of KN046 to CTLA-4 is expected to augment activation and proliferation of T-cells.

(b) Constitutive over-expression of CTLA-4 on tumor resident Tregs contributes to suppressive functions on T-cells. Binding of the anti-CTLA-4 sdAb of KN046 to CTLA-4 is expected to reduce Treg-mediated immunosuppression in tumor-related micro-environment.

(c) PD-L1 interacts with PD-1 to suppress activated T-cells. Tumors upregulate PD-L1 and obstruct T-cell function. Binding of the anti-PD-L1 sdAb of KN046 to PD-L1 is expected to restore T-cell immune responses in tumor-related micro-environment.

As illustrated in the above diagram, KN046 is made of two different sdAbs and an Fc region. The sdAbs possess fully functional antigen-binding capacity with a small molecular weight and high stability. The two sdAbs of KN046 bind to PD-L1 (anti-PD-L1 sdAb) and CTLA-4 (anti-CTLA-4 IgG1 sdAb) and are expected to achieve a dual blockade effect. In

addition to the synergistic mechanisms of action of CTLA-4 blockade and PD-L1 blockade, we adopt the following design in engineering our KN046 with a purpose to further improve its safety and efficacy profiles.

(1) *Targeted drug delivery*. The CTLA-4 blockade can augment activation of T-cells not only in tumor-related sites, but sometimes also in healthy tissues, causing on-target off-tumor toxicity. Such toxicity could be much more severe with a PD-(L)1/CTLA-4 dual blockade due to the over-activation of the immune system. To reduce such toxicity, our KN046 is engineered to enable the anti-PD-L1 sdAb to dominate drug distribution in the body to achieve a targeted drug delivery to enrich KN046 in tumor-related micro-environment and reduce unwanted drug interaction with healthy tissues. See "—Potential Advantages of KN046 – Low toxicity." Because high expression of PD-L1 is often closely associated with the tumor-related micro-environment, we believe our innovative design causes the enrichment of KN046 in tumor-related micro-environments instead of in healthy tissues and limit the anti-CTLA-4 blockade to these micro-environments, thereby preventing over-activation of T-cells in healthy tissues and decreasing toxicity.

(2) *Different CTLA-4 binding epitope*. Unlike other CTLA-4 inhibitors that directly bind to the interface of CTLA-4 and B7 ligands to inhibit their interaction, the anti-CTLA-4 sdAb of our KN046 mainly binds outside the interface and blocks the CTLA-4/B7 ligands interaction with steric hindrance from the overhang of the complement determined region (CDR) loop. Such difference in binding epitope may lead to an improved safety profile.

(3) *Preservation of Fc-mediated effector functions.* The Fc region of antibodies can recruit immune cells and induce immune responses through Fc-mediated effector functions, which can destroy antigen-expressing target cells. Our KN046 preserves the full Fc functions for immune cell-mediated anti-tumor activities. Tumor resident suppressive Tregs have been found to overexpress CTLA-4, we believe the preserved Fc functions can deplete Tregs in the tumor-related micro-environment and further enhance the efficacy of our KN046.

Current Therapy and Limitations

PD-1, PD-L1 and CTLA-4 are the three clinically-validated immune checkpoints for immuno-oncology therapies. To date, all of the immune checkpoint inhibitors on the market are monospecific, and there are no approved BsAbs worldwide targeting both the PD-1/PD-L1 pathway and CTLA-4 checkpoint.

As of the Latest Practicable Date, there were six approved PD-(L)1 inhibitors on the market outside China, including three PD-1 inhibitors (BMS's Opdivo (nivolumab), Merck's Keytruda (pembrolizumab) and Sanofi S.A. and Regeneron Pharmaceuticals, Inc.'s Libtayo (cemiplimab)) and three PD-L1 inhibitors (AstraZeneca and MedImmune's Imfinzi (durvalumab), Roche and Genentech's Tecentriq (atezolizumab) and Merck KGaA and Pfizer's Bavencio (avelumab)). These PD-(L)1 inhibitors are approved for over ten indications, including NSCLC, SCLC, melanoma, urothelial carcinoma and gastric cancer. In addition, Yervoy (ipilimumab) is the only marketed CTLA-4 inhibitor worldwide. Yervoy is approved as a monotherapy or as a part of a combination therapy with Opdivo for melanoma, RCC and MSI-H or dMMR metastatic CRC. All of the foregoing immune checkpoint inhibitors are approved in the United States.

In China, no CTLA-4 or PD-L1 inhibitors had been approved as of the Latest Practicable Date. Five PD-1 inhibitors have been approved in China since the second half of 2018, including Opdivo for locally advanced or metastatic NSCLC without EGFR or ALK tumor aberration, Keytruda for unresectable or metastatic melanoma and EGFR/ALK negative metastatic non-squamous NSCLC, Junshi's Tuoyi (toripalimab) for unresectable, metastatic malignant melanoma, as well as Innovent's Tyvyt (sintilimab) and Hengrui's Ailituo (camrelizumab) for refractory Hodgkin's lymphoma.

The introduction of immune checkpoint inhibitors offers breakthrough treatment for certain cancer indications that previously lacked effective therapies. In 2018, global sales of immune checkpoint inhibitors reached US$20.7 billion, according to the CIC Report. However, many cancer patients have limited responses to PD-(L)1 or CTLA-4 inhibitors as monotherapies. Studies have shown less than 20% of all cancer patients have a clinically meaningful response to these approved PD-1 or PD-L1 inhibitors as a monotherapy, and Yervoy is approved as a monotherapy for melanoma only.

As a dual blockade therapy of PD-1 and CTLA-4, the combination of Opdivo and Yervoy captured market share due to its better efficacy. The combination therapy has been approved in the United States but not in China. To date, this dual blockade therapy has been approved for patients with unresectable or metastatic melanoma, intermediate or poor risk advanced RCC, and MSI-H or dMMR metastatic CRC. A number of clinical studies have demonstrated that the nivolumab (PD-1 inhibitor) and ipilimumab (CTLA-4 inhibitor) combination therapy is more effective than a monotherapy of each agent in different cancer types with details of the comparison results set forth as below.

Indication	Clinical study	Sample size	Type of therapy	ORR
1L metastatic melanoma	Phase III trial (NCT01844505)	314	Combination therapy (nivolumab and ipilimumab)	50%
		316	Nivolumab	40%
		315	Ipilimumab	14%
MSI-H/dMMR metastatic CRC	Phase II trial (NCT02060188)	119	Combination therapy (nivolumab and ipilimumab)	49%
		74	Nivolumab	32%
Advanced or metastatic RCC	Phase III trial (NCT02231749)	425	Combination therapy (nivolumab and ipilimumab)	42%
	Phase II trial (NCT01354431)	168	Nivolumab[(1)]	20% to 22%

Abbreviations: CRC = colorectal cancer, RCC = renal cell carcinoma, ORR = objective response rate, 1L = first-line, MSI-H = high microsatellite instability, dMMR = DNA mismatch repair.

(1) Not a head-to-head study.

Source: CIC Report

Despite the superior efficacy compared with monotherapies, the combination therapy of Opdivo and Yervoy has the following limitations:

- *Safety concerns.* A dual blockade therapy can be more toxic than single-agent blockade. See "—Mechanism of Action—(1) Targeted drug delivery." The following table sets forth select clinical safety results of the combination therapy.

					Safety profile at approved dose levels		
Indication	Clinical study	Sample size	Dosages	Type of therapy	Treatment-related TEAE at any grade	Grade ≥3 treatment-related TEAE	Treatment discontinuation due to toxicity intolerance
1L metastatic melanoma	Phase III trial (NCT01844505)	314	Nivolumab 1 mg/kg plus ipilimumab 3 mg/kg Q3W for four doses, followed by nivolumab 3 mg/kg Q3W	Combination therapy (nivolumab and ipilimumab)	96%	59%	40%
		316	Nivolumab 3 mg/kg Q2W	Nivolumab	86%	22%	13%
		315	Ipilimumab 3 mg/kg Q3W for four doses	Ipilimumab	86%	28%	15%
MSI-H/dMMR metastatic CRC	Phase II trial (NCT02060188)	119	Nivolumab 3 mg/kg plus ipilimumab 1 mg/kg Q3W for four doses, followed by nivolumab 3 mg/kg Q2W	Combination therapy (nivolumab and ipilimumab)	73%	32%	13%
		74	Nivolumab 3 mg/kg Q2W	Nivolumab	70%	20%	7%
Advanced or metastatic RCC	Phase III trial (NCT02231749)	425	Nivolumab 3 mg/kg plus ipilimumab 1 mg/kg Q3W for four doses, followed by nivolumab 3 mg/kg Q2W	Combination therapy (nivolumab and ipilimumab)	93%	46%	22%
	Phase II trial (NCT01354431)	168	Nivolumab 0.3, 2, or 10 mg/kg Q3W	Nivolumab[(1)]	73%	11%	7%

Abbreviations: CRC = colorectal cancer, RCC = renal cell carcinoma, 1L = first-line, MSI-H = high microsatellite instability, dMMR = DNA mismatch repair.

(1) Not a head-to-head study.

Source: CIC Report

- *Narrow therapeutic window*. Due to safety concerns, the approved dosages for the combination therapy of Opdivo and Yervoy is (i) 1.0 mg/kg of Opdivo and 3.0 mg/kg of Yervoy Q3W for four doses (up to 12 weeks) for unresectable or metastatic melanoma, and (ii) 3.0 mg/kg of Opdivo and 1.0 mg/kg of Yervoy Q3W for four doses (up to 12 weeks) for advanced RCC and MSI-H or dMMR metastatic CRC. The restrictions on treatment duration and drug exposure limit the effectiveness of the combination therapy.

Potential Advantages of KN046

As a dual blockade therapy, KN046 has potential efficacy advantages over single-agent immune checkpoint inhibitors, similar to the approved combination therapy. Compared with the combination therapy of Opdivo and Yervoy, our KN046 has the following potential advantages:

- *Low toxicity*. To address the toxicity concern of the combination therapy, our KN046 is engineered to bind at least 20-fold more tightly to PD-L1 than to CTLA-4. Such engineering enables the anti-PD-L1 sdAb of KN046 to dominate the drug distribution with the potential to reduce the on-target off-tumor toxicity. See "—Mechanism of Action—(1) Targeted drug delivery." The following table summarizes the major results related to the safety profile of our KN046 at 5.0 mg/kg Q2W (RP2D) in phase I clinical trials in Australia and China as of the Data Cut-off Date.

		Safety profile at 5.0 mg/kg Q2W (RP2D)		
Clinical trial	**Location**	**Treatment-related TEAEs at any grade**	**Grade ≥3 treatment-related TEAEs**	**Treatment discontinuation due to toxicity intolerance**
			% (n/N)	
Phase I (N=29)[(1)(2)]	Australia	62.1% (95% CI, 42.3% to 79.3%)	20.7% (95% CI, 8.0% to 39.7%)	6.9%
Phase I (N=22)[(1)(3)]	China	77.3% (95% CI, 54.7% to 92.2%)	4.5% (95% CI, 0.1% to 22.8%)	13.6%

(1) Represents the number of enrolled subjects receiving KN046 at the RP2D.

(2) In KN046-AUS-001 trial, the median duration of exposure of KN046 in the RP2D cohort was eight weeks ranging from two to 44 weeks, and 13 (44.8%) of subjects enrolled in the RP2D cohort had a treatment duration of at least 12 weeks.

(3) In KN046-CHN-001 trial, the median duration of exposure of KN046 in the RP2D cohort was six weeks ranging from two to 28 weeks, and one (4.5%) of subjects enrolled in the RP2D cohort had a treatment duration of at least 12 weeks.

Source: Internal clinical trial data

See "—Summary of Clinical Results—Phase I Clinical Trials—Phase I Clinical Trial in Australia (KN046-AUS-001)—Safety" and "—Summary of Clinical Results—Phase I Clinical Trials—Phase I Clinical Trial in China (KN046-CHN-001)—Safety." In addition, we have observed accelerated drug clearance of KN046 at a low drug concentration level. This indicates a quick clearance of our drug candidate in healthy tissues, which also reduces toxicity which may be caused by concentration of KN046 in healthy tissues.

- *Broad therapeutic window.* As of the Data Cut-off Date, the preliminary results of the phase I clinical trials in Australia and China demonstrated that the drug intolerance was not exacerbated by the increased treatment duration. Such results indicated a broad therapeutic window of our KN046, which translates to potential for promising efficacy due to higher and longer drug exposure. As of the Data Cut-off Date, in the phase I clinical trial in Australia, 23 (43.4%) enrolled subjects had a treatment duration of at least 12 weeks, and only one out of the 23 subjects discontinued treatment due to treatment-related TEAEs. As of the same date, in the phase I clinical trial in China, 26 (40.0%) enrolled subjects had a treatment duration of at least 12 weeks, and none of the 26 subjects discontinued treatment due to treatment-related TEAEs. The following table sets forth information related to the therapeutic window of KN046 observed in the phase I clinical trials.

		All dose levels							
		All periods				Patients with treatment duration ≥ 12 weeks			
			Treatment discontinuation				Treatment discontinuation		
Clinical trial	Location	Patients enrolled	due to toxicity intolerance[1]	not due to toxicity intolerance[1]	Still on Treatment	Patients enrolled	due to toxicity intolerance[1]	not due to toxicity intolerance[1]	Still on Treatment
		(N1)		*n1 (%[2])*		*(N2)*		*n2 (%[3])*	
Phase I (N=53)	Australia	53	5 (9.4%)	23 (43.4%)	25 (47.2%)	23	1 (4.4%)	5 (21.7%)	17 (73.9%)
Phase I (N=65)	China	65	6 (9.2%)	25 (38.5%)	34 (52.3%)	26	0 (0)	7 (26.9%)	19 (73.1%)

(1) Toxicity intolerance refers to treatment-related TEAEs.

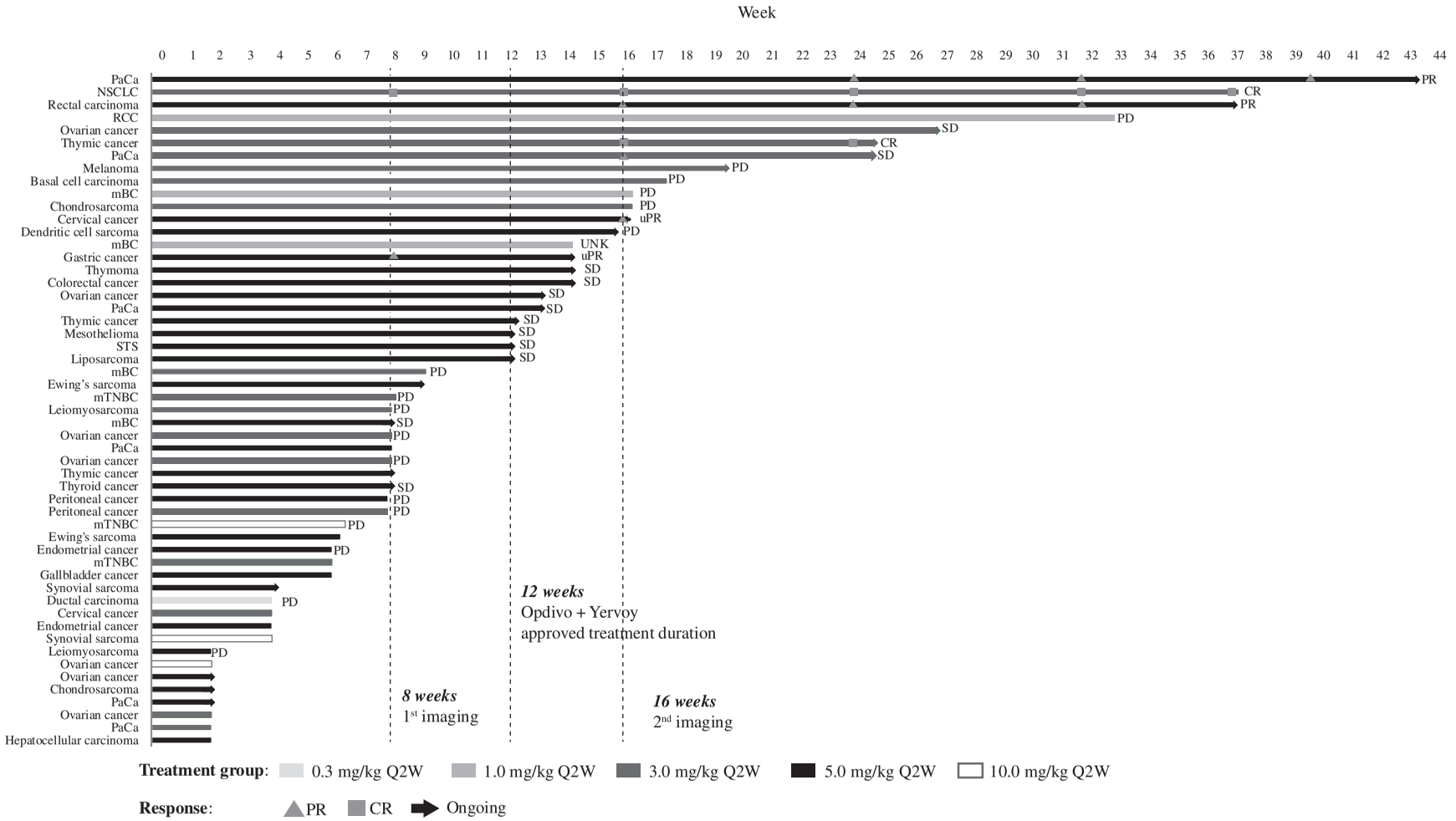
(2) Represents n1 divided by N1.

(3) Represents n2 divided by N2.

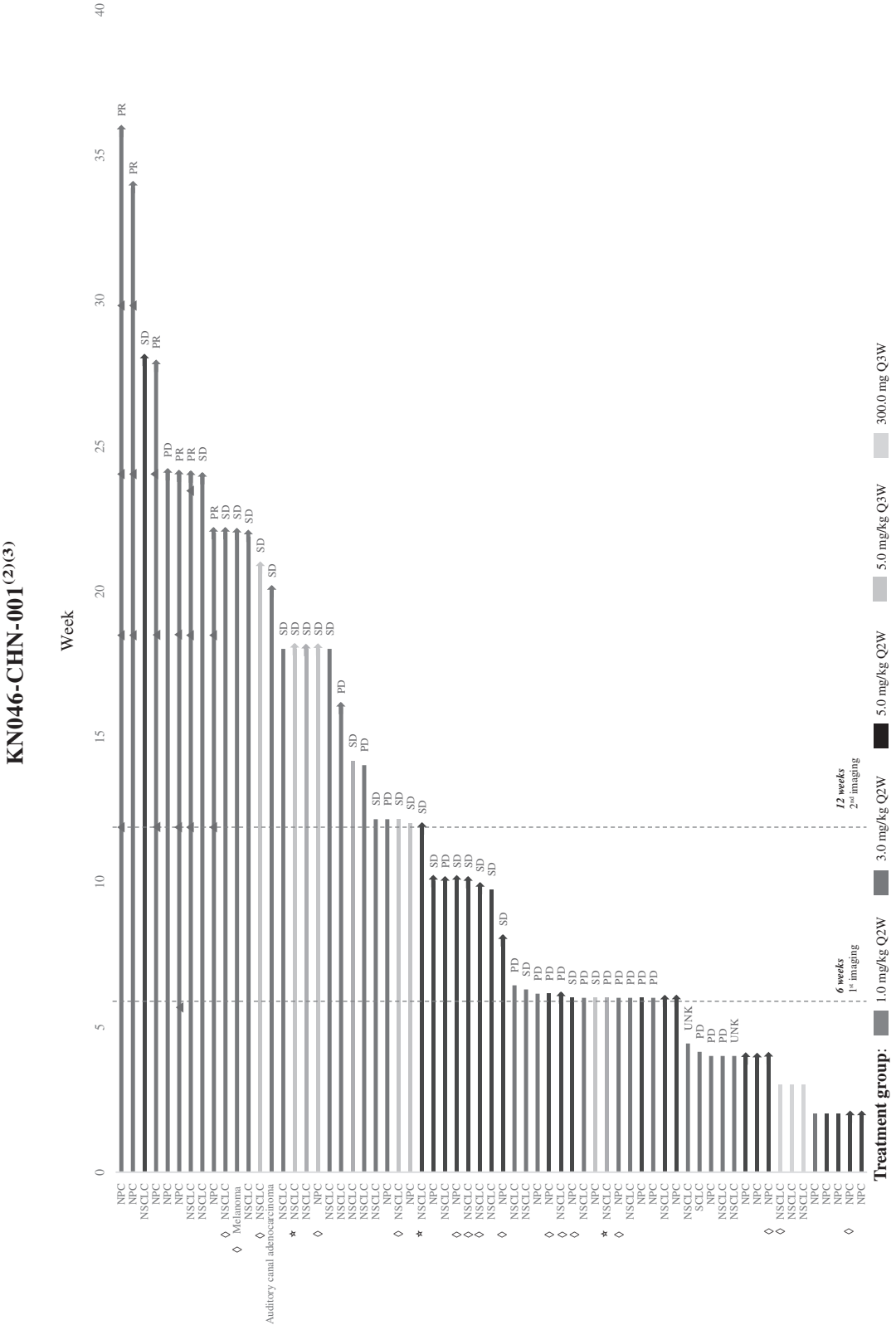
Source: Internal clinical trial data

The following swimming lane graphs illustrate the treatment duration and the best overall responses of all the enrolled subjects in the phase I clinical trials in Australia and China as of the Data Cut-off Date.

KN046-AUS-001



KN046-CHN-001[2][3]



Abbreviations: CR = complete response, PR = partial response, uPR = unconfirmed partial response, SD = stable disease, PD = progressive disease, NE = not evaluable, UNK = unknown, NSCLC = non-small cell lung cancer, RCC = renal cell carcinoma, mBC = metastatic breast cancer, STS = soft tissue sarcoma, mTNBC = metastatic triple-negative breast cancer, PaCa = pancreatic cancer, NPC = nasopharyngeal cancer, SCLC = small cell lung cancer.

◊ Failed prior anti-PD-1 treatment.

☆ Failed prior anti-OX40 treatment.

(1) The two subjects had SD. However, according to the protocol, the two subjects are categorized as unknown status.

(2) The enrollment of NSCLC subjects did not exclude patients with EGFR mutation and ALK translocation.

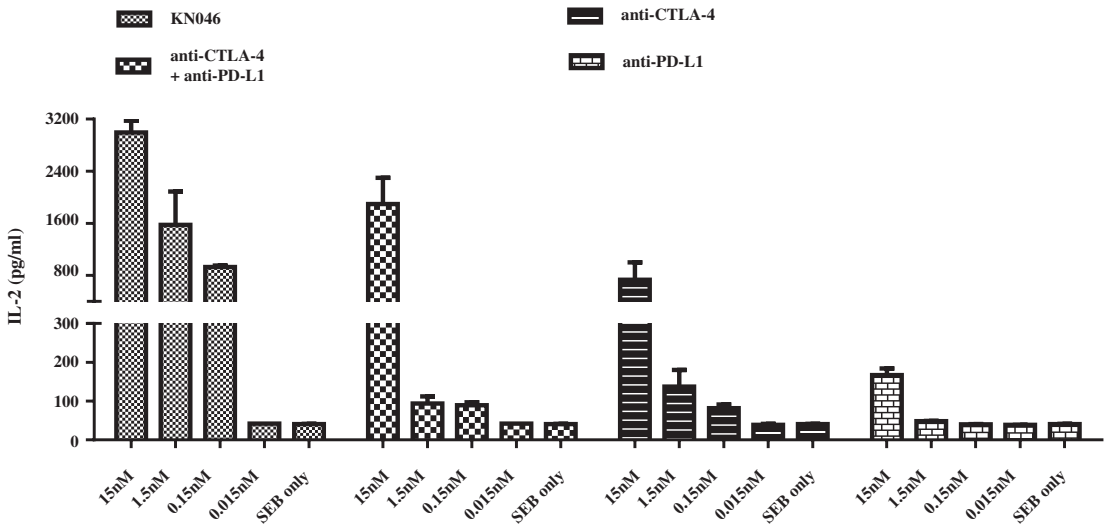
(3) 19 (29.2%) of the 65 enrolled subjects had failed prior immune checkpoint inhibitor treatments.

Source: Internal clinical trial data

Pre-clinical Studies

Synergistic Effect on T-cell Stimulation Assay (SEB-PBMC)

The purpose of this study was to investigate the synergistic effect of our KN046 on T-cell activation. Staphylococcal enterotoxin B (SEB) is a superantigen, which can activate peripheral blood mononuclear cell (PBMC) and trigger systemic release of pro-inflammatory cytokines such as IL-2. In this study, human PBMC was cultured with SEB in the presence of KN046, an anti-CTLA-4 monospecific control with the same CTLA-4 binding moiety of KN046, an anti-PD-L1 monospecific control with the same PD-L1 binding moiety of KN046, and a combination of the two monospecific controls at various concentration levels ranging from 0.015nM to 15nM for five days. The level of secretion of IL-2 was used to evaluate the activation of T-cells in this assay. The study showed that our KN046 was able to induce SEB-mediated IL-2 secretion in a dose-dependent manner. At the same concentration level, KN046 induced a higher IL-2 secretion level in comparison with the control groups, which may translate to better efficacy. The following graph illustrates the higher IL-2 secretion induced by KN046 compared to each control group.



* nM refers to concentration of added drugs, equivalent to the unit of nanomoles per liter (i.e. nmol/L).

Source: IND Application File to NMPA

Summary of Clinical Results

Phase I Clinical Trials

We are conducting a phase I clinical trial for our KN046 in Australia (KN046-AUS-001), which is subdivided into two parts, a phase Ia dose escalation study and a phase Ib dose expansion study. We conduct clinical trials in Australia because of its fast and efficient regulatory pathway for clinical trials with attractive government tax incentives. In addition, the ethnically diverse population in Australia enables us to conduct an early ethnic sensitivity

analysis between Caucasians and Chinese, and we may leverage Australia data to support and accelerate our clinical development in China and the United States. We initiated the KN046-AUS-001 trial in June 2018 and completed subject enrollment for this trial in October 2019. We are currently in the phase Ib study in Australia. In addition, we commenced a dose escalation study of a phase I clinical trial (KN046-CHN-001) in China in December 2018. This dose escalation phase is a bridging study to leverage the data from the Australia trial to accelerate the clinical trial process in China, one of our major target markets. We have completed the dose escalation study of KN046-CHN-001 trial and we initiated the dose expansion study in China in July 2019.

Phase I Clinical Trial in Australia (KN046-AUS-001)

KN046-AUS-001 is an open-label phase I clinical trial in Australia, consisting of a multiple-ascending phase Ia dose escalation study and a phase Ib dose expansion study. In February 2019, we concluded dose escalation in the 3 mg/kg and 5 mg/kg Q2W cohorts and determined the 5.0 mg/kg Q2W cohort to be the RP2D and BED. We started the phase Ib study at the RP2D afterwards. In parallel, we continued to conduct the dose escalation study in the 10 mg/kg Q2W cohort to determine the MTD of KN046. The phase Ia study has been completed and the phase Ib study was ongoing. As of the Data Cut-off Date, 53 subjects were enrolled in this phase I clinical trial and had received at least one dose of KN046 per treatment.

Study purpose. The primary objectives of the phase I clinical trial were to determine the MTD or BED and/or RP2D of KN046 as a single agent administered in subjects with metastatic or locally advanced solid tumors. The secondary objectives were to evaluate the preliminary anti-tumor activities and to characterize PK profile of our KN046.

Study design. The phase Ia dose escalation study adopted a classic "3+3" design, with up to 3 to 6 subjects treated at each dose level depending upon the incidence of DLT. Subjects received KN046 across five cohorts at 0.3 mg/kg, 1.0 mg/kg, 3.0 mg/kg, 5.0 mg/kg and 10.0 mg/kg Q2W intravenously. The phase Ib dose expansion study would be conducted based on the results of the phase Ia study, and the dose levels were determined to be 3.0 mg/kg Q2W and 5.0 mg/kg Q2W. The planned size of cohorts (including the dose escalation study and dose expansion study) at 1.0 mg/kg, 3.0 mg/kg and 5.0 mg/kg is up to 30 subjects, and the planned size of the cohort at 10.0 mg/kg is three to six subjects. Safety and tolerability would be assessed by monitoring TEAEs. Tumor assessments would be performed according to RECIST version 1.1.

Safety. As of the Data Cut-off Date, a total of 53 subjects were included in the safety data analysis, including 16 and 37 subjects enrolled in the phase Ia and phase Ib studies, respectively. The results have exhibited a favorable safety profile of our KN046 across all the cohorts. The available safety data of the KN046-AUS-001 trial showed that KN046-related TEAEs at grade 3 or higher levels were numerically lower than that of the approved combination therapy of Opdivo and Yervoy in (i) its phase III registration clinical trial (NCT01844505) for metastatic melanoma (59%); and (ii) its phase III registration clinical trial (NCT02231749) for advanced or metastatic RCC (46%). These incidence rates should be considered in light of the fact that they are not from head-to-head studies.

As of the Data Cut-off Date, 25 subjects remained on the study treatment. A total of 28 subjects had discontinued treatment, including:

- 15 subjects due to disease progression;
- three subjects withdraw their consent for the clinical trial we previously obtained;
- five subjects due to treatment-unrelated TEAEs, including one leading to death; and
- five subjects due to six treatment-related TEAEs, including two grade 3 immune-related hepatic function abnormal, one grade 2 alanine aminotransferase increased, one grade 3 arthritis, one grade 3 aspartate aminotransferase increased and one grade 3 colitis. These subjects completely recovered after treatment discontinuation.

The median duration of exposure of KN046 was eight weeks, ranging from two to 44 weeks. Four DLT events were observed in three subjects, including (i) one subject with grade 3 treatment-related hepatic function abnormal without bilirubin increased from the 5.0 mg/kg Q2W cohort; and (ii) one subject with grade 3 pruritic erythematous rash, and one subject with grade 3 aspartate aminotransferase increased and one grade 3 arthritis from the 10.0 mg/kg Q2W cohort. The relevant subjects recovered within three weeks. 17, 29 and 3 subjects were enrolled into the 3.0 mg/kg Q2W cohort, 5.0 mg/kg Q2W cohort and 10.0 mg/kg Q2W cohort, respectively. MTD was reached at 5.0 mg/kg. 5.0 mg/kg Q2W were determined to be the BED and RP2D.

As of the Data Cut-off Date, 37 (69.8%) out of the 53 subjects had experienced treatment-related TEAE of all grades, and 15 (28.3%) subjects had experienced treatment-related TEAEs at grade 3 or higher levels. 13 (24.5%) subjects had experienced treatment-related SAEs and 24 (45.3%) subjects had experienced irAEs, 11 (20.8%) of which were grade 3 or higher levels. Details of the TEAEs observed from all 53 subjects enrolled in the KN046-AUS-001 trial as of the Data Cut-off Date are summarized in the following table.

TEAE categories[1]	**0.3 mg/kg Q2W (N=1)**	**1.0 mg/kg Q2W (N=3)**	**3.0 mg/kg Q2W (N=17)**	**5.0 mg/kg Q2W (N=29)**	**10.0 mg/kg Q2W (N=3)**	**Total (N=53)**
			n (%)			
All TEAEs	1 (100%)	3 (100%)	17 (100%)	27 (93.1%)	3 (100%)	51 (96.2%)
TEAE, Grade ≥ 3	0	2 (66.7%)	13 (76.5%)	14 (48.3%)	3 (100%)	32 (60.4%)
Treatment-related TEAEs	1 (100%)	2 (66.7%)	13 (76.5%)	18 (62.1%)	3 (100%)	37 (69.8%)
Treatment-related TEAEs, Grade ≥ 3	0	2 (66.7%)	4 (23.5%)	6 (20.7%)	3 (100%)	15 (28.3%)
SAEs[2]	0	1 (33.3%)	11 (64.7%)	14 (48.3%)	2 (66.7%)	28 (52.8%)
Treatment-related SAEs[3]	0	1 (33.3%)	4 (23.5%)	6 (20.7%)	2 (66.7%)	13 (24.5%)

TEAE categories[1]	0.3 mg/kg Q2W (N=1)	1.0 mg/kg Q2W (N=3)	3.0 mg/kg Q2W (N=17)	5.0 mg/kg Q2W (N=29)	10.0 mg/kg Q2W (N=3)	Total (N=53)
			n (%)			
IrAEs	0	2 (66.7%)	9 (52.9%)	10 (34.5%)	3 (100%)	24 (45.3%)
IrAEs, Grade ≥ 3	0	1 (33.3%)	3 (17.6%)	4 (13.8%)	3 (100%)	11 (20.8%)
TEAEs leading to permanent treatment discontinuation	0	1 (33.3%)	2 (11.8%)	6 (20.7%)	1 (33.3%)	10 (18.9%)
Treatment-related TEAEs leading to permanent treatment discontinuation	0	1 (33.3%)	1 (5.9%)	2 (6.9%)	1 (33.3%)	5 (9.4%)
Treatment-related TEAE leading to death	0	0	0	0	0	0

(1) Reported under National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
(2) The most frequent SAEs (n≥2) included infusion-related reaction (n=3, 5.7%), arthritis (n=2, 3.8%), diarrhoea (n=2, 3.8%), lower respiratory tract infection (n=2, 3.8%), pneumonia (n=2, 3.8%), pulmonary embolism (n=2, 3.8%) and pyrexia (n=2, 3.8%).
(3) Including infusion-related reaction (n=3, 5.7%), arthritis (n=2, 3.8%), hepatic function abnormal (n=1, 1.9%), immune-mediated enterocolitis (n=1, 1.9%), hypersensitivity (n=1, 1.9%), adrenal insufficiency (n=1, 1.9%), colitis (n=1, 1.9%), hepatitis (n=1, 1.9%), myalgia (n=1, 1.9%), myositis (n=1, 1.9%), rash pruritic (n=1, 1.9%) and gastritis (n=1, 1.9%).

Source: Internal clinical trial data

The table below summarizes the most frequent treatment-related TEAEs in the KN046-AUS-001 trial based on clinical trial data as of the Data Cut-off Date (all grades ≥10%, or any ≥grade 3).

	0.3 mg/kg Q2W (N=1)		1.0 mg/kg Q2W (N=3)		3.0 mg/kg Q2W (N=17)		5.0 mg/kg Q2W (N=29)		10.0 mg/kg Q2W (N=3)		Total (N=53)	
Treatment-related TEAEs by Preferred Term[1]	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥ 3	All grades	Grade ≥3
						n (%)						
Arthralgia	0	0	1 (33.3%)	0	4 (23.5%)	0	2 (6.9%)	0	0	0	7 (13.2%)	0
Infusion-related reaction	0	0	0	0	4 (23.5%)	0	2 (6.9%)	1 (3.4%)	0	0	6 (11.3%)	1 (1.9%)
Fatigue	0	0	0	0	0	0	4 (13.8%)	0	1 (33.3%)	1 (33.3%)	5 (9.4%)	1 (1.9%)
Pruritus	0	0	0	0	3 (17.6%)	1 (5.9%)	2 (6.9%)	0	0	0	5 (9.4%)	1 (1.9%)
Alanine aminotransferase increased	0	0	0	0	1 (5.9%)	0	1 (3.4%)	1 (3.4%)	2 (66.7%)	0	4 (7.5%)	1 (1.9%)
Arthritis	0	0	0	0	2 (11.8%)	1 (5.9%)	0	0	2 (66.7%)	1 (33.3%)	4 (7.5%)	2 (3.8%)
Hepatic function abnormal	0	0	1 (33.3%)	1 (33.3%)	0	0	1 (3.4%)	1 (3.4%)	0	0	2 (3.8%)	2 (3.8%)

Treatment-related TEAEs by Preferred Term[(1)]	0.3 mg/kg Q2W (N=1)		1.0 mg/kg Q2W (N=3)		3.0 mg/kg Q2W (N=17)		5.0 mg/kg Q2W (N=29)		10.0 mg/kg Q2W (N=3)		Total (N=53)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥ 3	All grades	Grade ≥3
	n (%)											
Rash pruritic	0	0	0	0	1 (5.9%)	0	0	0	1 (33.3%)	1 (33.3%)	2 (3.8%)	1 (1.9%)
Abdominal pain lower	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0	0	0	1 (1.9%)	1 (1.9%)
Immune-mediated enterocolitis	0	0	0	0	0	0	1 (3.4%)	1 (3.4%)	0	0	1 (1.9%)	1 (1.9%)
Aspartate aminotransferase increased	0	0	0	0	0	0	1 (3.4%)	0	2 (66.7%)	1 (33.3%)	3 (5.7%)	1 (1.9%)
Adrenal insufficiency	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	0	0	1 (1.9%)	1 (1.9%)
Colitis	0	0	0	0	0	0	1 (3.4%)	1 (3.4%)	0	0	1 (1.9%)	1 (1.9%)
Gastroesophageal reflux disease	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	0	0	1 (1.9%)	1 (1.9%)
Myositis	0	0	0	0	0	0	1 (3.4%)	1 (3.4%)	0	0	1 (1.9%)	1 (1.9%)

(1) Medical Dictionary for Regulatory Activities Preferred Terms.

Treatment-related TEAEs occurred in 37 patients, 15 of which were at grade 3 or higher levels. The most frequent treatment-related TEAEs included arthralgia and infusion-related reaction. The treatment-related TEAEs were not found to occur in a dose-dependent manner, and neither the number nor severity of treatment-related TEAEs was exacerbated due to dose escalation at the RP2D or lower dose levels.

The table below summarizes the irAEs in the KN046-AUS-001 trial based on clinical trial data as of the Data Cut-off Date (all grades ≥ 5%, or any ≥ grade 3).

IrAEs by System Organ Class and Preferred Term[(1)]	0.3 mg/kg Q2W (N=1)		1.0 mg/kg Q2W (N=3)		3.0 mg/kg Q2W (N=17)		5.0 mg/kg Q2W (N=29)		10.0 mg/kg Q2W (N=3)		Total (N=53)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
	n (%)											
Any	0	0	2 (66.7%)	1 (33.3%)	9 (52.9%)	3 (17.6%)	10 (34.5%)	4 (13.8%)	3 (100%)	3 (100%)	24 (45.3%)	11 (20.8%)
Skin and subcutaneous tissue disorders	0	0	0	0	4 (23.5%)	0	3 (10.3%)	0	1 (33.3%)	1 (33.3%)	8 (15.1%)	1 (1.9%)
Pruritus	0	0	0	0	3 (17.6%)	0	1 (3.4%)	0	0	0	4 (7.5%)	0
Rash pruritic	0	0	0	0	1 (5.9%)	0	0	0	1 (33.3%)	1 (33.3%)	2 (3.8%)	1 (1.9%)
Musculoskeletal and connective tissue disorders	0	0	1 (33.3%)	0	3 (17.6%)	1 (5.9%)	2 (6.9%)	0	2 (66.7%)	1 (33.3%)	8 (15.1%)	2 (3.8%)
Arthralgia	0	0	1 (33.3%)	0	2 (11.8%)	0	1 (3.4%)	0	0	0	4 (7.5%)	0
Arthritis	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	2 (66.7%)	1 (33.3%)	3 (5.7%)	2 (3.8%)
Myalgia	0	0	0	0	1 (5.9%)	0	1 (3.4%)	0	1 (33.3%)	0	3 (5.7%)	0

IrAEs by System Organ Class and Preferred Term[1]	0.3 mg/kg Q2W (N=1)		1.0 mg/kg Q2W (N=3)		3.0 mg/kg Q2W (N=17)		5.0 mg/kg Q2W (N=29)		10.0 mg/kg Q2W (N=3)		Total (N=53)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
	n (%)											
Investigations	0	0	0	0	2 (11.8%)	0	4 (13.8%)	1 (3.4%)	1 (33.3%)	1 (33.3%)	7 (13.2%)	2 (3.8%)
Transaminases increased	0	0	0	0	1 (5.9%)	0	3 (10.3%)	0	0	0	4 (7.5%)	0
Alanine aminotransferase increased	0	0	0	0	0	0	1 (3.4%)	1 (3.4%)	1 (33.3%)	0	2 (3.8%)	1 (1.9%)
Blood lactate dehydrogenase increased	0	0	0	0	0	0	0	0	1 (33.3%)	1 (33.3%)	1 (1.9%)	1 (1.9%)
Gastrointestinal disorders	0	0	1 (33.3%)	0	3 (17.6%)	1 (5.9%)	2 (6.9%)	2 (6.9%)	0	0	6 (11.3%)	3 (5.7%)
Colitis	0	0	0	0	0	0	1 (3.4%)	1 (3.4%)	0	0	1 (1.9%)	1 (1.9%)
Gastritis	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	0	0	1 (1.9%)	1 (1.9%)
Gastroesophageal reflux disease	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	0	0	1 (1.9%)	1 (1.9%)
Immune-mediated enterocolitis	0	0	0	0	0	0	1 (3.4%)	1 (3.4%)	0	0	1 (1.9%)	1 (1.9%)
Endocrine disorders	0	0	1 (33.3%)	0	3 (17.6%)	1 (5.9%)	0	0	0	0	4 (7.5%)	1 (1.9%)
Adrenal insufficiency	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	0	0	1 (1.9%)	1 (1.9%)
Hepatobiliary disorders	0	0	1 (33.3%)	1 (33.3%)	1 (5.9%)	0	2 (6.9%)	1 (3.4%)	0	0	4 (7.5%)	2 (3.8%)
Hepatic function abnormal	0	0	1 (33.3%)	1 (33.3%)	0	0	1 (3.4%)	1 (3.4%)	0	0	2 (3.8%)	2 (3.8%)
General disorders and administration site conditions	0	0	0	0	1 (5.9%)	0	0	0	1 (33.3%)	1 (33.3%)	2 (3.8%)	1 (1.9%)
Fatigue	0	0	0	0	0	0	0	0	1 (33.3%)	1 (33.3%)	1 (1.9%)	1 (1.9%)
Renal and urinary disorders	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	0	0	1 (1.9%)	1 (1.9%)
Renal impairment	0	0	0	0	1 (5.9%)	1 (5.9%)	0	0	0	0	1 (1.9%)	1 (1.9%)

(1) Medical Dictionary for Regulatory Activities System Organ Class and Preferred Terms.

IrAEs occurred in 24 patients, 11 of which were at grade 3 or higher levels. Skin and subcutaneous tissue disorders and musculoskeletal and connective tissue disorders were the most frequent irAEs. The irAEs were not found to occur in a dose-dependent manner, and neither the number nor severity of irAEs was exacerbated due to dose escalation at the RP2D or lower levels.

Efficacy. In general, all of the subjects enrolled in this study had previously failed standard-of-care treatments. As of the Data Cut-off Date, there were 35 evaluable subjects. The efficacy results showed that among, the 35 evaluable subjects, two subjects had confirmed CRs, two had confirmed PRs, two had unconfirmed PRs and 12 had SD. Evaluable subjects refer to patients who had measurable diseases at baseline and completed at least one post-baseline tumor assessment as of the Data Cut-off Date. 20 of the evaluable subjects remained on the study treatment as of Data Cut-off Date. 18 enrolled subjects who had not reached the first post-baseline tumor assessment as of the Data Cut-off Date were excluded.

The table below summarizes the best overall response in the efficacy analysis of the KN046-AUS-001 trial.

Response	0.3 mg/kg Q2W (N=1)	1.0 mg/kg Q2W (N=2)	3.0 mg/kg Q2W (N=13)	5.0 mg/kg Q2W[(1)] (N=18)	10.0 mg/kg Q2W (N=1)	Total (N=35)
			n (%)			
Confirmed CR	0	0	2 (15.4%)	0	0	2 (5.7%)
Unconfirmed CR	0	0	0	0	0	0
Confirmed PR	0	0	0	2 (11.1%)	0	2 (5.7%)
Unconfirmed PR	0	0	0	2 (11.1%)	0	2 (5.7%)
SD	0	0	2 (15.4%)	10 (55.6%)	0	12 (34.3%)
PD	1 (100%)	2 (100%)	9 (69.2%)	4 (22.2%)	1 (100%)	17 (48.6%)
CR[(2)]+PR[(2)]	0	0	2 (15.4%)	4 (22.2%)	0	6 (17.1%)
DCR (CR[(2)]+PR[(2)]+SD[(3)])	0	0	4 (30.8%)	14 (77.8%)	0	18 (51.4%)
Target Lesion Shrinkage	0	0	5 (38.5%)	10 (55.6%)	0	15 (42.9%)

Abbreviations: CR=complete response, PR=partial response, SD=stable disease, PD=progressive disease, DCR=disease control rate.

(1) 5.0 mg/kg Q2W was determined to be the RP2D.

(2) Including confirmed and unconfirmed responses.

(3) Lasted for at least six weeks.

Source: Internal clinical trial data

The following table further sets forth details of the best overall response at various scans and number of lines of prior treatment received of the 35 evaluable subjects based on clinical trial data as of the Data Cut-off Date.

Patient No.	Classified response (as of the Data Cut-off Date)	Change of target lesions from baseline (%)	Duration of treatments (days)	End of patient treatment (Yes/No)	Change of target lesions from baseline at respective tumor assessment cycle (%)												Cancer indication type/ Primary tumor sites	Cohort	Number of lines of prior treatment	Prior immune check point inhibitor treatment(s)
					1		2		3		4		5		6					
1[(1)]	CR	(100%)	253	Y	CR	(100%)	CR	(100%)	CR	(100%)	CR	(100%)	CR	(100%)	PD	(100%)	NSCLC	3.0 mg/kg Q2W	1	-
2[(2)]	CR	(100%)	168	N	SD	(24%)	CR	(100%)	CR	(100%)	-	-	-	-	-	-	Thymic cancer	3.0 mg/kg Q2W	1	-
3[(3)]	PR	(87%)	252	N	SD	4%	PR	(35%)	PR	(87%)	PR	(78%)	-	-	-	-	Rectal carcinoma	5.0 mg/kg Q2W	3	-
4[(4)]	PD	(56%)	56	Y	PR	(56%)	-	-	-	-	-	-	-	-	-	-	Ovarian cancer	3.0 mg/kg Q2W	4	-
5[(5)]	uPR	(50%)	98	N	PR	(50%)	-	-	-	-	-	-	-	-	-	-	Gastric cancer	5.0 mg/kg Q2W	3	-
6[(5)]	uPR	(49%)	111	N	SD	(19%)	PR	(49%)	-	-	-	-	-	-	-	-	Cervical cancer	5.0 mg/kg Q2W	1	-
7[(6)]	PR	(41%)	308	N	SD	3%	SD	(12%)	PR	(32%)	PR	(41%)	PR	(38%)	-	-	Pancreatic cancer	5.0 mg/kg Q2W	2	-
8	SD	(36%)	168	N	SD	(27%)	PR	(36%)	PD	2%	-	-	-	-	-	-	Pancreatic cancer	3.0 mg/kg Q2W	3	-
9	SD	(29%)	85	N	SD	(29%)	-	-	-	-	-	-	-	-	-	-	Thymic cancer	5.0 mg/kg Q2W	1	-
10	SD	(29%)	84	N	SD	(29%)	-	-	-	-	-	-	-	-	-	-	Mesothelioma	5.0 mg/kg Q2W	0	-
11	SD	(13%)	91	N	SD	(13%)	-	-	-	-	-	-	-	-	-	-	Ovarian cancer	5.0 mg/kg Q2W	4	-
12	SD	(9%)	91	N	SD	(9%)	-	-	-	-	-	-	-	-	-	-	Pancreatic cancer	5.0 mg/kg Q2W	0	-
13[(7)]	PD	(8%)	55	Y	SD	(8%)	-	-	-	-	-	-	-	-	-	-	Peritoneal Cancer	5.0 mg/kg Q2W	2	-
14	SD	(8%)	183	N	SD	(6%)	SD	(8%)	-	-	-	-	-	-	-	-	Ovarian cancer	3.0 mg/kg Q2W	2	-
15	SD	(1%)	98	N	SD	(1%)	-	-	-	-	-	-	-	-	-	-	Colorectal cancer	5.0 mg/kg Q2W	1	-
16	SD	2%	84	N	SD	2%	-	-	-	-	-	-	-	-	-	-	Liposarcoma	5.0 mg/kg Q2W	3	-
17	SD	3%	56	N	SD	3%	-	-	-	-	-	-	-	-	-	-	Thyroid cancer	5.0 mg/kg Q2W	1	-
18	SD	4%	56	N	SD	4%	-	-	-	-	-	-	-	-	-	-	Breast cancer	5.0 mg/kg Q2W	3	-
19	SD	5%	98	N	SD	5%	-	-	-	-	-	-	-	-	-	-	Thymoma	5.0 mg/kg Q2W	1	-
20	SD	5%	84	N	SD	5%	-	-	-	-	-	-	-	-	-	-	Soft tissue sarcoma	5.0 mg/kg Q2W	1	-
21	PD	21%	28	Y	PD	21%	-	-	-	-	-	-	-	-	-	-	Breast cancer	0.3 mg/kg Q2W	2	-
22	PD	22%	56	Y	PD	22%	PD	22%	-	-	-	-	-	-	-	-	Leiomyosarcoma	3.0 mg/kg Q2W	2	-
23	PD	28%	64	Y	PD	28%	-	-	-	-	-	-	-	-	-	-	Breast cancer	3.0 mg/kg Q2W	3	CD40/PD-1

Patient No.	Classified response (as of the Data Cut-off Date)	Change of target lesions from baseline (%)	Duration of treatments (days)	End of patient treatment (Yes/No)	Change of target lesions from baseline at respective tumor assessment cycle (%)												Cancer indication type/ Primary tumor sites	Cohort	Number of lines of prior treatment	Prior immune check point inhibitor treatment(s)
					1		2		3		4		5		6					
24	PD	30%	112	Y	PD	30%	PD	67%	PD	67%	-	-	-	-	-	-	Chondrosarcoma	3.0 mg/kg Q2W	0	-
25	PD	31%	108	N	PD	31%	SD	17%	-	-	-	-	-	-	-	-	Dendritic Cell Sarcoma	5.0 mg/kg Q2W	4	-
26	PD	32%	224	Y	PD	32%	SD	32%	SD	32%	SD	32%	-	-	-	-	Renal cell carcinoma	1.0 mg/kg Q2W	2	PD-1
27	PD	33%	120	N	PD	33%	PD	67%	-	-	-	-	-	-	-	-	Basal cell carcinoma	3.0 mg/kg Q2W	1	-
28	PD	37%	55	Y	PD	37%	-	-	-	-	-	-	-	-	-	-	Peritoneal Cancer	3.0 mg/kg Q2W	4	-
29	PD	38%	134	N	PD	38%	PD	77%	PD	100%	-	-	-	-	-	-	Melanoma	3.0 mg/kg Q2W	2	PD-1
30	PD	46%	42	Y	PD	46%	-	-	-	-	-	-	-	-	-	-	Endometrial cancer	5.0 mg/kg Q2W	1	-
31	PD	46%	14	Y	PD	46%	-	-	-	-	-	-	-	-	-	-	Leiomyosarcoma	5.0 mg/kg Q2W	1	-
32	PD	63%	56	Y	PD	63%	-	-	-	-	-	-	-	-	-	-	Ovarian cancer	3.0 mg/kg Q2W	6	-
33	PD	73%	57	Y	PD	73%	-	-	-	-	-	-	-	-	-	-	Breast cancer	3.0 mg/kg Q2W	2	-
34	PD	92%	112	Y	PD	92%	PD	146%	-	-	-	-	-	-	-	-	Breast cancer	1.0 mg/kg Q2W	2	-
35	PD	102%	45	Y	PD	102%	-	-	-	-	-	-	-	-	-	-	Breast cancer	10.0 mg/kg Q2W	3	-

Abbreviations: CR=complete response, PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response, NSCLC = non-small cell lung cancer, mBC=metastatic breast cancer, PD-1=anti-PD-1 treatment(s), CD40=anti-CD40 treatment(s).

(1) This subject was classified as a confirmed CR with 100% reduction of target lesion from baseline through five assessment cycles. However, the subject had PD on the sixth assessment due to development of new lesions and was no longer on the study treatment as of the Data Cut-off Date.

(2) The subject was classified as complete response according to EDC standard, whereby target lesion remained non-detectable in two subsequent scans, albeit obscured by radiation fibrosis.

(3) The subject achieved a confirmed PR after one SD and three PR observed through four assessment cycles.

(4) Reduction of target lesion was observed in this subject in the first tumor assessment, but the subject developed a new lesion and was confirmed as a PD.

(5) The subject achieved at least one PR and classified as an unconfirmed PR.

(6) The subject achieved a confirmed PR after two SD and three PRs observed through five assessment cycles.

(7) Despite reduction of target lesion, the subject had PD due to non-target lesion unequivocal progression.

The key findings from the table above is that continuing anti-tumor effect has been observed in a number of subjects over a longer treatment duration as evaluated by multiple scans, including subjects that had received two or more lines of prior therapy. Specifically:

- Two confirmed CRs occurred in one NSCLC subject and one thymic cancer subject from the 3.0 mg/kg Q2W cohort. The NSCLC subject showed the CR through five scans over a treatment duration of 36 weeks, and the thymic cancer subject showed a confirmed CR after one SD and two CRs observed through three scans over a treatment duration of 24 weeks;

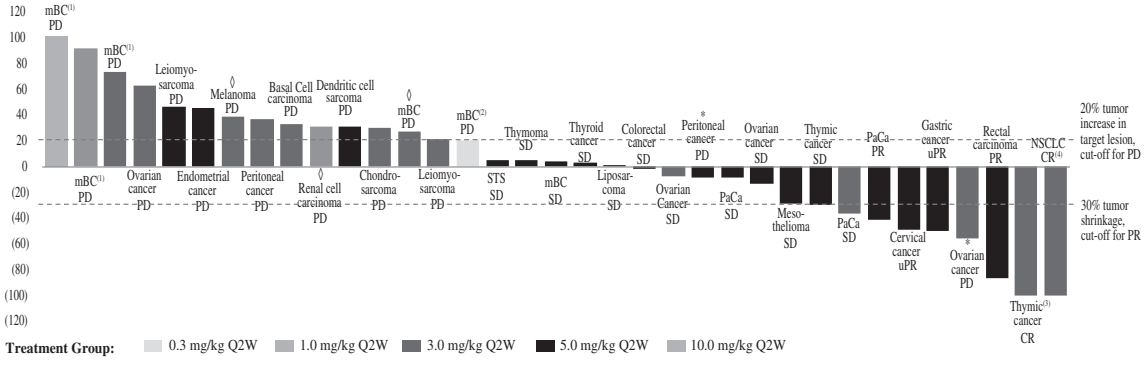
- Four PRs (including two confirmed ones and two unconfirmed ones) occurred in subjects of various indications, including pancreatic cancer and rectum cancer. Although studies have shown that pancreatic cancer and rectum cancer tend not to respond positively to PD-(L)1 inhibitors, the preliminary results of the KN046-AUS-001 trial have shown early efficacy signals in these two cancers as well as other cancers, including (i) one confirmed PR that occurred in a subject with metastatic pancreatic cancer from the 5.0 mg/kg Q2W cohort (on treatment for approximately 44 weeks as of the Data Cut-off Date, treatment ongoing); (ii) one confirmed PR that occurred in a subject with rectum cancer from the 5.0 mg/kg Q2W cohort (on treatment for approximately 36 weeks as of the Data Cut-off Date, treatment ongoing); (iii) one unconfirmed PR that occurred in a subject with gastric cancer from the 5.0 mg/kg Q2W cohort (on treatment for approximately 14 weeks as of the Data Cut-off Date, treatment ongoing); and (iv) one unconfirmed PR that occurred in a subject with cervical cancer from the 5.0 mg/kg Q2W cohort (on treatment for approximately 16 weeks as of the Data Cut-off Date, treatment ongoing);

- SD occurred in 12 subjects, including conspicuous reduction in the size of target lesion diagnosed in seven subjects based on the first assessment; and

- Six out of the seven subjects who had the longest treatment duration (between 24 to 44 weeks) all had reduction in target lesion, including two confirmed CRs, two confirmed PRs, two SD and one PD in classified response. The last one was one RCC subject, who had the fourth longest treatment duration (32 weeks). This subject was classified as PD upon the first assessment but demonstrated target lesion control with SD through the three subsequent scans.

The following waterfall plot shows the best overall response of the 35 evaluable subjects receiving KN046 as measured by percentage of change of target lesions from baseline based on CT/MRI scans.

Tumor Target Lesion Shrinkage from Baseline (%)

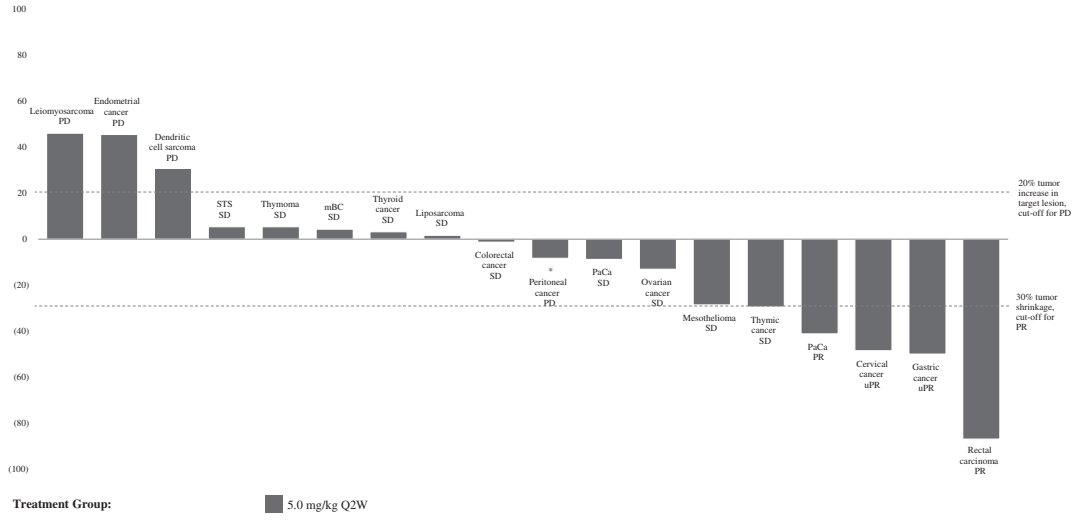


Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response, mBC=metastatic breast cancer, PaCa = pancreatic cancer.
* Denotes new lesion(s) or non-target lesion(s) unequivocal progression.
◊ Failed prior anti-PD-1 treatment.
(1) All were TNBC.
(2) Hormone receptor positive mBC.
(3) The subject was classified as complete response according to EDC standard, whereby target lesion remains non-detectable in two subsequent scans, albeit obscured by radiation fibrosis.
(4) The subject showed the CR through five scans over a treatment duration of 36 weeks (253 days).

Source: Internal clinical trial data

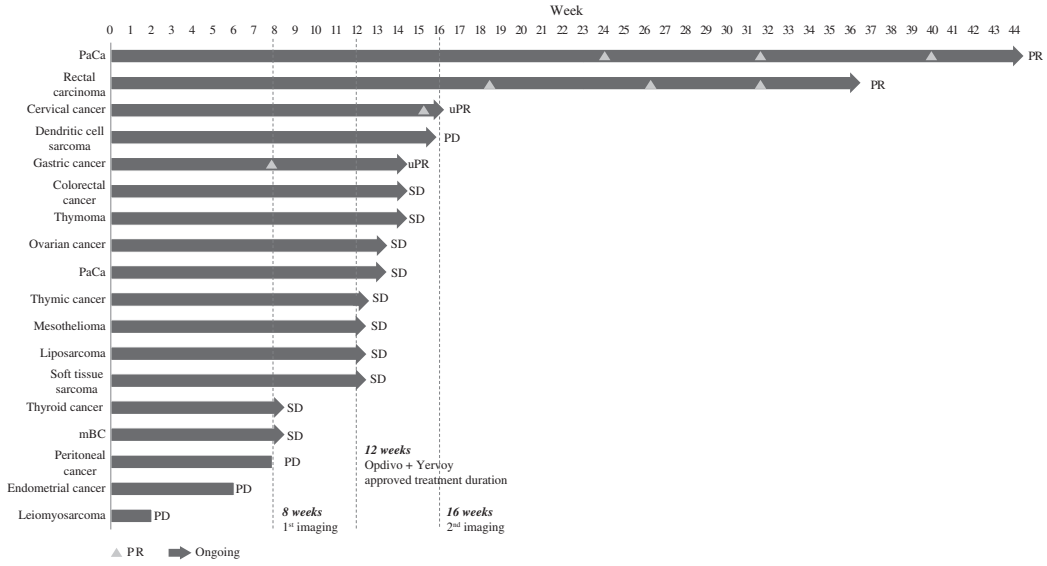
The RP2D in KN046-AUS-001 trial was determined to be 5.0 mg/kg Q2W. Among the 18 evaluable subjects in the RP2D cohort, the DCR was 77.8% and 10 (55.6%) subjects had target lesion shrinkage. The following waterfall plot shows the best overall response of the 18 evaluable subjects receiving KN046 at the RP2D as measured by percentage of change of target lesions from baseline based on CT/MRI scans.

Tumor Target Lesion Shrinkage from Baseline (%)



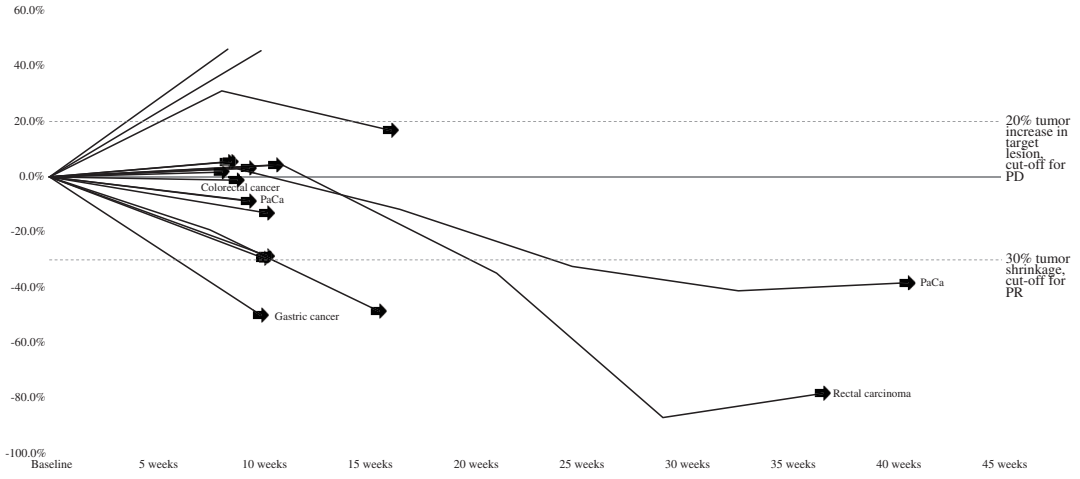
Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response, mBC=metastatic breast cancer, STS = soft tissue sarcoma, PaCa = pancreatic cancer.
* Denotes new lesion.
Source: Internal clinical trial data

As of the Data Cut-off Date, the efficacy results in the 5.0 mg/kg Q2W (RP2D) cohort demonstrated a broad therapeutic window of KN046. 13 out of the 18 evaluable subjects in this cohort have been on treatment for at least 12 weeks treatment ongoing, including two PRs, two uPRs and eight SD. The following swimming lane graph illustrates the treatment duration and the best overall responses of the evaluable subjects in the RP2D cohort as of the Data Cut-off Date.



Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response, mBC=metastatic breast cancer, PaCa = pancreatic cancer.
Source: Internal clinical trial data

The following spider plot shows the change of target lesions across treatment duration of the 18 evaluable subjects receiving KN046 at the RP2D as of the Data Cut-off Date. As illustrated in the spider plot, two confirmed PRs (a pancreatic cancer subject and a rectal carcinoma subject) and two unconfirmed PRs (a gastric cancer subject and a cervical cancer subject) were among the top five subjects in terms of treatment duration, suggesting that the efficacy signals were improved over the treatment duration.



PK profile. As of the Data Cut-off Date, PK profiles following the first 60 or 90 minutes of infusion and dose proportionality of KN046 have been characterized in 40 subjects of the KN046-AUS-001 trial. The results showed a favorable PK profile to support a Q2W or Q3W schedule. Average half-life of KN046 in the 3.0 mg/kg cohort and 5.0 mg/kg cohort was approximately seven days. Linear PK was shown at higher dose levels from 1.0 mg/kg to 10.0 mg/kg.

Conclusion. Our KN046 exhibited a favorable safety profile in subjects with advanced solid tumors and the preliminary efficacy results demonstrated promising anti-tumor activities.

Phase I Clinical Trial in China (KN046-CHN-001)

We are conducting an open-label phase I clinical trial (KN046-CHN-001) in China, which consists of a dose escalation study followed by a cohort expansion study in multiple solid tumors and hematological malignancy indications. The dose escalation study was initiated in December 2018. As of the Data Cut-off Date, 65 subjects were enrolled in the dose escalation and had received at least one dose of KN046 per treatment. In July 2019, we initiated the dose expansion study.

Study purpose. The primary objectives of the dose escalation study are to determine the MTD and/or RP2D to establish dosing regimens to achieve better safety and efficacy profile for KN046. The secondary objectives of the dose escalation study are to evaluate the preliminary anti-tumor activities and characterize the PK profile of our KN046. This dose

escalation study is a bridging study to demonstrate that our KN046 is not sensitive to ethnic factors in terms of drug safety, tolerability and PK observed in the dose escalation study of KN046-CHN-001 trial and the phase Ia study of the KN046-AUS-001 trial. The dose escalation study is intended to bridge the data from the phase Ia study of the KN046-AUS-001 trial to the Chinese population, which will support the subsequent clinical trials of KN046 we intend to conduct in China.

The primary objectives of the dose expansion study are to establish the clinical activity of our KN046 as a monotherapy in selected indications. The secondary objectives are to confirm the safety profile observed during the dose escalation study and characterize PK profile of KN046.

Study design. The dose escalation study adopted a modified toxicity probability interval design. Subjects received KN046 intravenously across five cohorts, including 1.0 mg/kg, 3.0 mg/kg and 5.0 mg/kg Q2W, and 5.0 mg/kg and 300.0 mg flat dose Q3W.

The dose expansion study is expected to be conducted after the dose escalation study. The dose level was determined to be 3.0 mg/kg and 5.0 mg/kg Q2W or Q3W based on the results of the dose escalation study. A number of cohorts are planned to assess the efficacy, safety and predictive biomarker of KN046, including but not limited to (i) second-line or later-line treatment of unresectable/metastatic melanoma; (ii) second-line or later-line treatment of unresectable/metastatic NPC; (iii) second-line treatment of unresectable/metastatic urothelial cancer; and (iv) second-line treatment of extensive stage SCLC. We have adopted an adaptive design which allows indication expansion based on available clinical data from time to time.

Safety and tolerability would be assessed by monitoring TEAEs. Tumor assessments for solid tumors would be performed according to RECIST version 1.1. Tumor assessments for lymphomas were performed according to Lugano 2014.

Safety. As of the Data Cut-off Date, 65 subjects enrolled in the dose escalation study were included in the safety data analysis. The results have exhibited favorable safety profile of our KN046 and the safety results showed no significant differences from the KN046-AUS-001 trial.

As of the Data Cut-off Date, 34 subjects remained on the study treatment. A total of 31 subjects had discontinued treatment including:

- 20 subjects due to disease progression;
- one subject due to loss of follow-up;
- two subjects due to clinical deterioration, including one in the opinion of the investigator treatment discontinuation would be the best, and one clinical progression. None of these deterioration cases were treatment-related;
- two subjects due to treatment-unrelated TEAEs; and

- six subjects due to treatment-related TEAE, including (i) four infusion-related reactions, two of which were grade 3; (ii) one grade 3 hypersensitivity; and (iii) one death, which occurred on a late-stage NSCLC subject from the 300 mg Q3W cohort with baseline massive pleural fluid and a history of heart disease. The investigator was not be able to determine the reason for the death; however, the death was reported as a treatment-related TEAE according to the clinical design protocol.

The median duration of exposure of KN046 was approximately 10 weeks, ranging from two to 36 weeks. No subjects experienced DLTs. MTD was not reached at 5.0 mg/kg. 5.0 mg/kg Q2W was determined to be the RP2D.

As of the Data Cut-off Date, 55 (84.6%) out of the 65 subjects had experienced treatment-related TEAE of all grades and nine (13.9%) subjects had experienced treatment-related TEAEs at grade 3 or higher levels. Four (6.2%) subjects experienced treatment-related SAE. 32 (49.2%) subjects had experienced irAEs, two (3.1%) were grade 3. Details of the TEAEs observed from all 65 subjects are summarized in the following table.

TEAE categories[1]	1.0 mg/kg Q2W (N=1)	3.0 mg/kg Q2W (N=30)	5.0 mg/kg Q2W (N=22)	5.0 mg/kg Q3W (N=6)	300.0 mg Q3W (N=6)	Total (N=65)
			n (%)			
All TEAEs	1 (100%)	30 (100%)	21 (95.5%)	6 (100%)	6 (100%)	64 (98.5%)
TEAE, Grade ≥ 3	1 (100%)	12 (40.0%)	3 (13.6%)	1 (16.7%)	4 (66.7%)	21 (32.3%)
Treatment-related TEAEs	1 (100%)	27 (90.0%)	17 (77.3%)	6 (100%)	4 (66.7%)	55 (84.6%)
Treatment-related TEAEs, Grade ≥ 3	0	6 (20.0%)	1 (4.5%)	1 (16.7%)	1 (16.7%)	9 (13.9%)
SAEs[2]	1 (100%)	7 (23.3%)	2 (9.1%)	0	4 (66.7%)	14 (21.5%)
Treatment-related SAEs[3]	0	3 (10.0%)	0	0	1 (16.7%)	4 (6.2%)
IrAEs	0	18 (60.0%)	9 (40.9%)	5 (83.3%)	0	32 (49.2%)
IrAEs, Grade ≥ 3	0	2 (6.7%)	0	0	0	2 (3.1%)
TEAEs leading to permanent treatment discontinuation	0	2 (6.7%)	3 (13.6%)	1 (16.7%)	2 (33.3%)	8 (12.3%)
Treatment-related TEAEs leading to permanent treatment discontinuation	0	2 (6.7%)	3 (13.6%)	0	1 (16.7%)	6 (9.2%)
Treatment-related TEAE leading to death	0	0	0	0	1 (16.7%)	1 (1.5%)

(1) Reported under National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0.
(2) 14 subjects experienced 17 SAEs, including death (n=2, 3.1%) (including one death for which the investigator was not able to determine the reason for the death and was reported as treatment-related TEAE according to the clinical design protocol, and one death that was determined to be treatment-unrelated by the investigator), infusion-related reaction (n=2, 3.1%), infection (n=1, 1.5%), bone pain (n=1, 1.5%), tachypnea (n=1, 1.5%), hemoptysis (n=1, 1.5%), rash (n=1, 1.5%), fever (n=1, 1.5%), hemorrhoids bleeding (n=1, 1.5%), hepatic insufficiency (n=1, 1.5%), acute respiratory distress syndrome (n=1, 1.5%), immune-mediated pneumonitis (n=1, 1.5%), brain edema (n=1, 1.5%), cardiac arrest (n=1, 1.5%) and pleural effusion (n=1, 1.5%).
(3) Four subjects experienced six treatment-related SAEs, including rash (n=1, 1.5%), infusion-related reaction (n=2, 3.1%, one subject experienced twice), immune-mediated pneumonitis (n=1, 1.5%) and one death (n=1, 1.5%) (see note 2).

Source: Internal clinical trial data

The table below summarizes the most frequent treatment-related TEAEs in the KN046-CHN-001 trial based on clinical trial data as of the Data Cut-off Date (all grades ≥10%, or any≥grade 3).

Treatment-related TEAEs by Preferred Term[(1)]	1.0 mg/kg Q2W (N=1)		3.0 mg/kg Q2W (N=30)		5.0 mg/kg Q2W (N=22)		5.0 mg/kg Q3W (N=6)		300.0 mg Q3W (N=6)		Total (N=65)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
	n (%)											
Rash	0	0	13 (43.3%)	2 (6.7%)	7 (31.8%)	0	3 (50.0%)	0	0	0	23 (35.4%)	2 (3.1%)
Pruritus	0	0	9 (30.0%)	0	6 (27.3%)	0	3 (50.0%)	0	1 (16.7%)	0	19 (29.2%)	0
Alanine aminotransferase elevation	0	0	9 (30.0%)	0	1 (4.5%)	0	1 (16.7%)	0	1 (16.7%)	0	12 (18.5%)	0
Infusion-related reaction	0	0	6 (20.0%)	2 (6.7%)	4 (18.2%)	1 (4.5%)	2 (33.3%)	0	0	0	12 (18.5%)	3 (4.6%)
Fatigue	0	0	7 (23.3%)	0	1 (4.5%)	0	3 (50.0%)	0	0	0	11 (16.9%)	0
Aspartate aminotransferase elevation	0	0	6 (20.0%)	0	1 (4.5%)	0	2 (33.3%)	1 (16.7%)	1 (16.7%)	0	10 (15.4%)	1 (1.5%)
Hyponatremia	0	0	3 (10.0%)	2 (6.7%)	0	0	0	0	0	0	3 (4.6%)	2 (3.1%)
Anemia	0	0	2 (6.7%)	1 (3.3%)	0	0	0	0	0	0	2 (3.1%)	1 (1.5%)
Hypersensitivity	0	0	1 (3.3%)	1 (3.3%)	0	0	0	0	0	0	1 (1.5%)	1 (1.5%)
Death	0	0	0	0	0	0	0	0	1 (16.7%)	1 (16.7%)	1 (1.5%)	1 (1.5%)

(1) Under Medical Dictionary for Regulatory Activities Preferred Terms.

The table below summarizes the irAEs in the KN046-CHN-001 trial based on clinical trial data as of the Data Cut-off Date (all grades ≥ 5%, or any ≥ grade 3).

IrAEs by System Organ class and Preferred Term[(1)]	1.0 mg/kg Q2W (N=1)		3.0 mg/kg Q2W (N=30)		5.0 mg/kg Q2W (N=22)		5.0 mg/kg Q3W (N=6)		300.0 mg Q3W (N=6)		Total (N=65)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
	n (%)											
Any	0	0	18 (60.0%)	2 (6.7%)	9 (40.9%)	0	5 (83.3%)	0	0	0	32 (49.2%)	2 (3.1%)
Skin and subcutaneous tissue disorders	0	0	15 (50.0%)	2 (6.7%)	8 (36.4%)	0	3 (50.0%)	0	0	0	26 (40.0%)	2 (3.1%)
Rash	0	0	12 (40.0%)	2 (6.7%)	6 (27.3%)	0	3 (50.0%)	0	0	0	21 (32.3%)	2 (3.1%)
Pruritus	0	0	8 (26.7%)	0	6 (27.3%)	0	2 (33.3%)	0	0	0	16 (24.6%)	0
General disorders and administration site conditions	0	0	3 (10.0%)	0	0	0	2 (33.3%)	0	0	0	5 (7.7%)	0
Fatigue	0	0	3 (10.0%)	0	0	0	2 (33.3%)	0	0	0	5 (7.7%)	0

(1) Under Medical Dictionary for Regulatory Activities System Organ Class and Preferred Terms.

Similar to the results of the KN046-AUS-001 trial, neither the treatment-related TEAEs nor the irAEs in the dose escalation study of the KN046-CHN-001 trial were found to occur in a dose-dependent manner.

Efficacy. In general, the subjects enrolled in the KN046-CHN-001 trial had previously failed standard-of-care treatments. As of the Data Cut-off Date, there were 50 evaluable subjects. The efficacy analysis showed that, among the 50 evaluable subjects, six had confirmed PRs and 26 had SD. 15 enrolled subjects who had not reached the first post-baseline tumor assessment were excluded. 27 of the evaluable subjects remained on the study treatment as of the Data Cut-off Date.

The table below summarizes the best overall response in the efficacy analysis of the KN046-CHN-001 trial as of the Data Cut-off Date.

Response	1.0 mg/kg Q2W (N=1)	3.0 mg/kg Q2W (N=27)	5.0 mg/kg Q2W[(1)] (N=13)	5.0 mg/kg Q3W (N=6)	300.0 mg Q3W (N=3)	Total (N=50)
			n (%)			
Confirmed CR	0	0	0	0	0	0
Unconfirmed CR	0	0	0	0	0	0
Confirmed PR	0	6 (22.2%)	0	0	0	6 (12.0%)
Unconfirmed PR	0	0	0	0	0	0
SD	0	9 (33.3%)	9 (69.2%)	6 (100%)	2 (66.7%)	26 (52.0%)
PD	1 (100%)	12 (44.4%)	4 (30.8%)	0	1 (33.3%)	18 (36.0%)
CR[(2)] + PR[(2)]	0	6 (22.2%)	0	0	0	6 (12.0%)
DCR (CR[(2)]+PR[(2)]+SD[(3)])	0	15 (55.6%)	9 (69.2%)	6 (100%)	2 (66.7%)	32 (64.0%)
Target Lesion Shrinkage	0	12 (44.4%)	4 (30.8%)	3 (50.0%)	1 (33.3%)	20 (40.0%)

Abbreviations: CR=complete response, PR=partial response, SD=stable disease, PD=progressive disease, DCR=disease control rate.

(1) 5.0 mg/kg Q2W was determined to be the RP2D.

(2) Including confirmed and unconfirmed responses.

(3) Lasted for at least six weeks.

Source: Internal clinical trial data

The following table further sets forth details of the best overall response at various scans and number of lines of prior treatment received of the 50 evaluable subjects as of the Data Cut-off Date.

Patient No.[1]	Classified response (as of the Data Cut-off Date)	Change of target lesions from baseline (%)	Duration of treatments (days)	End of patient treatment (Yes/No)	Change of target lesions from baseline at respective tumor assessment cycle (%)												Cancer indication type/ Primary tumor sites	Cohort	Number of lines of prior treatment	Prior immune checkpoint inhibitor treatment(s)
					1		2		3		4		5		6					
1	PR	(70%)	251	N	SD	(24%)	PR	(58%)	PR	(64%)	PR	(70%)	PR	(65%)	–	–	NPC	3.0 mg/kg Q2W	3	–
2	PR	(58%)	168	N	PR	(35%)	PR	(51%)	PR	(58%)	–	–	–	–	–	–	NPC	3.0 mg/kg Q2W	1	–
3	PR	(54%)	154	N	SD	(16%)	PR	(43%)	PR	(54%)	–	–	–	–	–	–	NPC	3.0 mg/kg Q2W	1	–
4	PR	(49%)	168	N	SD	(17%)	PR	(35%)	PR	(44%)	PR	(49%)	–	–	–	–	NSCLC	3.0 mg/kg Q2W	2	–
5	PR	(38%)	237	N	SD	(2%)	SD	(27%)	PR	(38%)	PR	(33%)	PR	(35%)	–	–	NPC	3.0 mg/kg Q2W	1	–
6	PR	(36%)	195	N	SD	(26%)	PR	(33%)	PR	(35%)	PR	(36%)	–	–	–	–	NPC	3.0 mg/kg Q2W	1	–
7	SD[6]	(23%)	83	N	SD	(23%)	–	–	–	–	–	–	–	–	–	–	NSCLC	5.0 mg/kg Q2W	4	OX40
8	SD	(13%)	126	Y	SD	(13%)	PD	8%	PD	25%	–	–	–	–	–	–	NSCLC	3.0 mg/kg Q2W	1	–
9	SD	(12%)	126	N	SD	(12%)	SD	(8%)	–	–	–	–	–	–	–	–	NSCLC	5.0 mg/kg Q3W	2	OX40
10	SD	(12%)	154	N	SD	(12%)	SD	(8%)	SD	(7%)	–	–	–	–	–	–	NSCLC	3.0 mg/kg Q2W	4	PD-1
11	SD	(12%)	126	N	SD	6%	SD	(12%)	–	–	–	–	–	–	–	–	NSCLC	300.0 mg Q3W	2	–
12	SD	(9%)	44	Y	SD	(9%)	–	–	–	–	–	–	–	–	–	–	NSCLC	3.0 mg/kg Q2W	2	–
13	SD	(9%)	126	N	SD	(9%)	SD	(8%)	–	–	–	–	–	–	–	–	NPC	5.0 mg/kg Q3W	5	PD-1
14[2]	SD	(9%)	85	Y	SD	(9%)	SD	18%	–	–	–	–	–	–	–	–	NSCLC	3.0 mg/kg Q2W	1	–
15	SD	(8%)	196	N	SD	4%	SD	(3%)	SD	(1%)	SD	(8%)	–	–	–	–	NSCLC	5.0 mg/kg Q2W	2	–
16	SD	(6%)	56	N	SD	(6%)	–	–	–	–	–	–	–	–	–	–	NPC	5.0 mg/kg Q2W	2	PD-1
17[3]	PD	(5%)	98	Y	SD	4%	SD	(5%)	SD	3%	–	–	–	–	–	–	NSCLC	3.0 mg/kg Q2W	1	–
18	SD	(3%)	146	N	SD	(3%)	SD	(0%)	SD	(0%)	–	–	–	–	–	–	NSCLC	5.0 mg/kg Q3W	6	PD-1
19	SD[6]	(2%)	42	Y	SD	(2%)	–	–	–	–	–	–	–	–	–	–	NPC	5.0 mg/kg Q2W	1	PD-1
20	SD	(1%)	154	N	SD	0%	SD	(1%)	SD	2%	–	–	–	–	–	–	Melanoma	3.0 mg/kg Q2W	3	PD-1
21	SD	0%	68	Y	SD	0%	SD	2%	–	–	–	–	–	–	–	–	NSCLC	5.0 mg/kg Q2W	1	–
22[4]	PD	0%	112	N	SD	0%	SD	(2%)	SD	0%	–	–	–	–	–	–	NSCLC	3.0 mg/kg Q2W	3	–
23	SD	1%	70	N	SD	1%	–	–	–	–	–	–	–	–	–	–	NPC	5.0 mg/kg Q2W	1	–
24[4]	PD	2%	70	N	SD	2%	–	–	–	–	–	–	–	–	–	–	NSCLC	5.0 mg/kg Q2W	1	–

Patient No.[1]	Classified response (as of the Data Cut-off Date)	Change of target lesions from baseline (%)	Duration of treatments (days)	End of patient treatment (Yes/No)	Change of target lesions from baseline at respective tumor assessment cycle (%)						Cancer indication type/ Primary tumor sites	Cohort	Number of lines of prior treatment	Prior immune checkpoint inhibitor treatment(s)
					1	2	3	4	5	6				
25	SD	3%	168	N	SD 3%	SD 15%	SD 15%	-	-	-	NSCLC	3.0 mg/kg Q2W	1	-
26	SD	5%	84	Y	SD 5%	SD 19%	-	-	-	-	NPC	5.0 mg/kg Q3W	3	-
27	SD	6%	126	Y	SD 6%	SD 10%	-	-	-	-	NSCLC	3.0 mg/kg Q2W	3	-
28	SD	6%	153	N	SD 6%	SD 13%	-	-	-	-	NSCLC	3.0 mg/kg Q2W	1	-
29	SD[6]	6%	69	N	SD 6%	-	-	-	-	-	NSCLC	5.0 mg/kg Q2W	3	PD-1
30	SD	7%	70	N	SD 7%	-	-	-	-	-	NPC	5.0 mg/kg Q2W	3	PD-1
31	SD	7%	140	N	SD 7%	SD 12%	SD 18%	-	-	-	Cancer of external auditory canal	3.0 mg/kg Q2W	0	-
32	PD	8%	42	Y	SD 8%	-	-	-	-	-	NSCLC	3.0 mg/kg Q2W	1	-
33[5]	PD	9%	45	Y	SD 9%	-	-	-	-	-	NSCLC	3.0 mg/kg Q2W	2	-
34	SD	9%	42	Y	SD 9%	-	-	-	-	-	NPC	5.0 mg/kg Q3W	2	-
35[5]	PD	10%	28	Y	SD 10%	-	-	-	-	-	NPC	3.0 mg/kg Q2W	2	-
36[4]	PD	10%	42	Y	SD 10%	-	-	-	-	-	NSCLC	300.0 mg Q3W	4	OX40
37[4]	PD	12%	43	Y	SD 12%	-	-	-	-	-	NPC	3.0 mg/kg Q2W	1	-
38	PD	12%	85	Y	SD 12%	PD 41%	-	-	-	-	NPC	3.0 mg/kg Q2W	3	-
39[4]	PD	13%	42	Y	SD 13%	-	-	-	-	-	NPC	3.0 mg/kg Q2W	3	PD-1
40	SD	14%	70	N	SD 14%	-	-	-	-	-	NSCLC	5.0 mg/kg Q2W	2	PD-1
41[4]	PD	15%	42	Y	SD 15%	-	-	-	-	-	NSCLC	3.0 mg/kg Q2W	2	-
42	SD	18%	99	N	SD 18%	PD 26%	-	-	-	-	NSCLC	300.0 mg Q3W	1	-
43	SD	19%	85	Y	SD 19%	PD 26%	-	-	-	-	NSCLC	5.0 mg/kg Q3W	5	PD-1
44	PD	24%	28	Y	PD 24%	-	-	-	-	-	NSCLC	3.0 mg/kg Q2W	1	-
45	PD	28%	169	N	PD 28%	SD 18%	PD 21%	PD 26%	-	-	NPC	3.0 mg/kg Q2W	1	-
46	PD	28%	43	Y	PD 28%	-	-	-	-	-	NPC	5.0 mg/kg Q2W	2	PD-1
47	PD	33%	42	Y	PD 33%	-	-	-	-	-	NPC	5.0 mg/kg Q2W	2	-
48	PD	33%	42	Y	PD 33%	-	-	-	-	-	NPC	3.0 mg/kg Q2W	4	-
49	PD	35%	29	Y	PD 35%	-	-	-	-	-	SCLC	1.0 mg/kg Q2W	2	-
50	PD	36%	43	N	PD 36%	-	-	-	-	-	NSCLC	5.0 mg/kg Q2W	2	PD-1

Abbreviations: PR=partial response, uPR=unconfirmed partial response, SD=stable disease, PD=progressive disease, NSCLC = non-small cell lung cancer, NPC = nasopharyngeal cancer, SCLC = small cell lung cancer, PD-1=anti-PD-1 treatment(s), OX40=anti-OX40 treatment(s).

(1) Two subjects who had first post baseline tumor assessment which were performed within six weeks are not listed. The two subjects had SD. However, according to the protocol, the two subjects were categorized as unknown status.

(2) Classified as SD for target lesion and overall response, albeit time point response during the second assessment was actually PD due to new lesion developed.

(3) The response of this subject in the first assessment was classified as unknown (SD observed in both target lesion and non-target lesion without development of new lesion based on scan within four weeks from the first assessment). Despite the SD observed in two subsequent scans on target lesion, the subject was classified as PD due to development of new lesions.

(4) Classified as PD due to development of new lesions despite SD observed on target lesion.

(5) Classified as PD due to development of new lesion and unequivocal progression in non-target lesion.

(6) Evaluated on the 41st day (imaging with ± 3 days tolerance).

Source: Internal clinical trial data

The following summarizes the key findings from the table above:

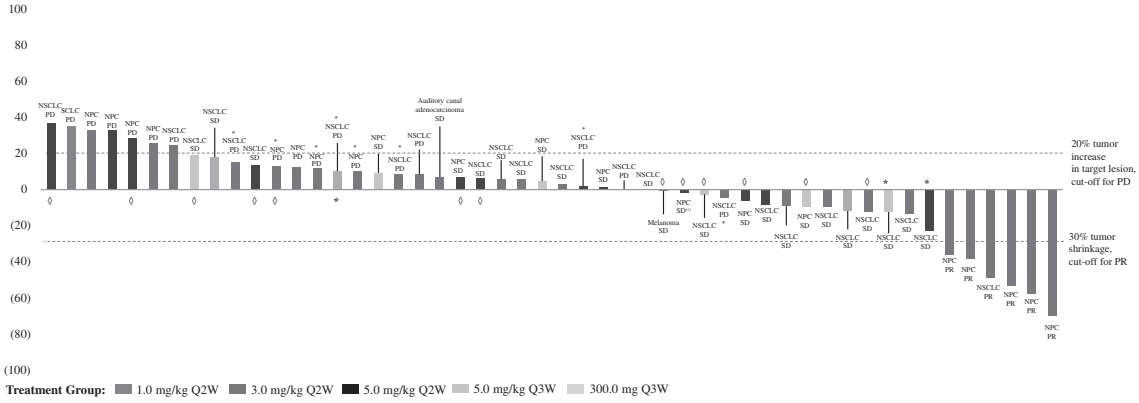
- Six confirmed PR were observed, including five NPC subjects and one NSCLC subject. All these subjects were from the 3.0 mg/kg Q2W cohort with treatment duration between 22 and 36 weeks through three to five assessment cycles;

- We had a total of 26 SD as of the Data Cut-off Date, including 17 NSCLC subjects, seven NPC subjects, one melanoma subject and one subject with cancer of the external auditory canal; and

- Among the 16 subjects that had failed prior immune checkpoint inhibitor treatments, including either PD-1 or OX40 inhibitors, 12 subjects were classified as SD, including seven NSCLC subjects, four NPC subjects and one melanoma subject.

The following waterfall plot shows the best overall response of the 50 evaluable subjects receiving KN046 as measured by percentage of change of target lesions from baseline based on CT/MRI scans as of the Data Cut-off Date.

Tumor Target Lesion Shrinkage from Baseline (%)[2][3]



Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response, NSCLC = non-small cell lung cancer, NPC = nasopharyngeal cancer, SCLC = small cell lung cancer.

* Denotes new lesion(s) or non-target lesion(s) unequivocal progression.

◇ Failed prior anti-PD-1 treatment.

☆ Failed prior anti-OX40 treatment.

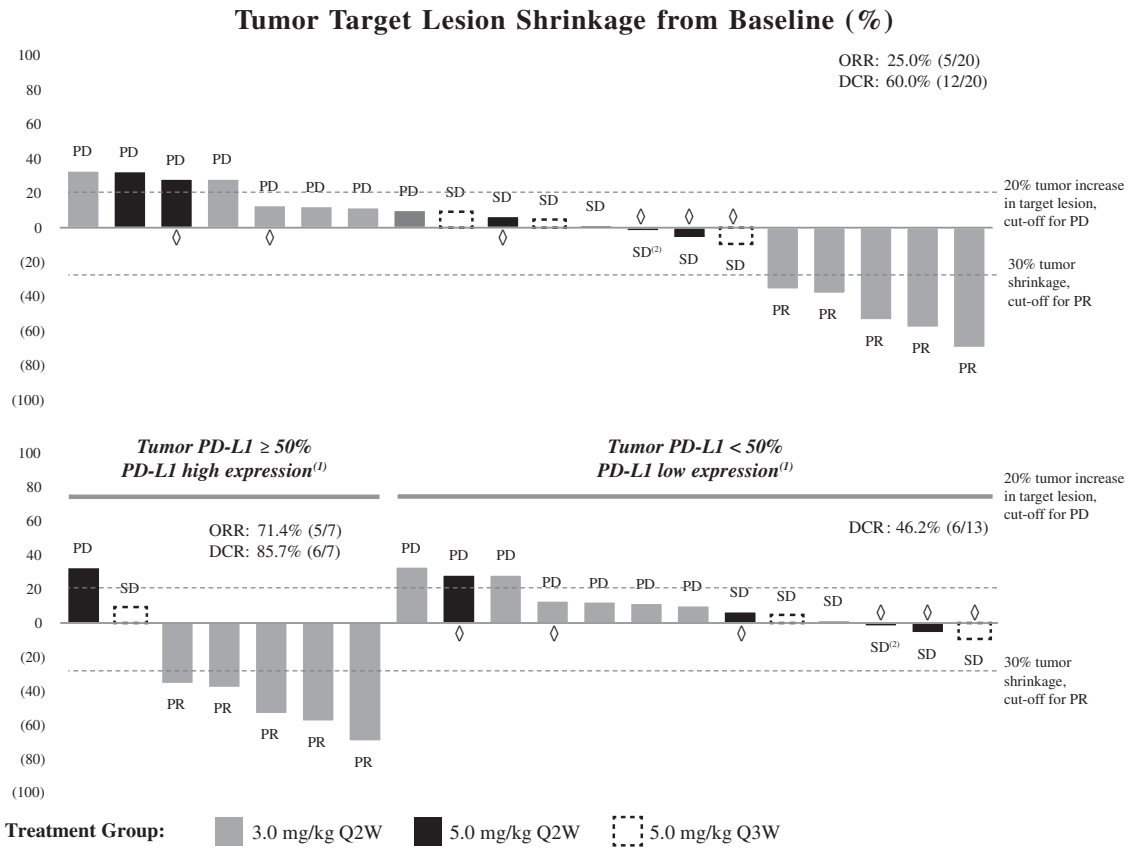
(1) Evaluated on the 41st day (imaging with ± 3 days tolerance).

(2) The enrollment of NSCLC subjects did not exclude subjects with EGFR mutation and ALK translocation.

(3) 16 (32.0%) of the 50 evaluable subjects had failed prior immune checkpoint inhibitor treatments.

Source: Internal clinical trial data

Based on available efficacy data, we observed early efficacy signals of KN046 on NPC. We had 20 evaluable NPC subjects as of Data Cut-off Date, although all these subjects have failed at least one-prior treatment line (including six subjects that failed PD-L1 inhibitor), we achieved a DCR of 60.0% and an ORR of 25.0%. In the evaluable NPC subjects that are anti-PD-(L)1 treatment naïve, the DCR was 57.1% and the ORR was 35.7%. The following waterfall plots show the best response of the evaluable NPC subjects receiving KN046 as measured by percentage of change of target lesions from baseline based on CT/MRI scans as of the Data Cut-off Date.



Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response, NPC = nasopharyngeal cancer.

◊ Failed prior anti-PD-1 treatment.

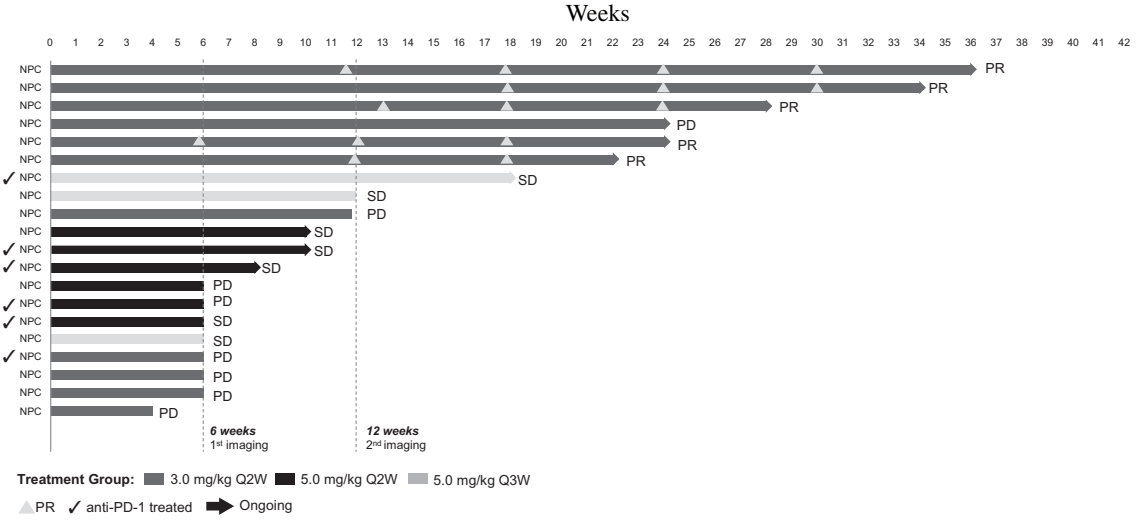
(1) PD-L1 expression level is determined using tumor proportion score, or TPS, the percentage of viable tumor cells showing partial or at tumor sites complete membrane staining at any intensity. A subject is considered to have low PD-L1 expression if TPS is below 50% and high PD-L1 expression if TPS is at or above 50%.

(2) Evaluated on the 41st day (imaging with ± 3 days tolerance).

Source: Internal clinical trial data

The waterfall plot distinguished by PD-L1 expression level showed that PD-L1 is a strong predictive biomarker. Strong correlation between tumor reduction and PD-L1 overexpression was observed and subjects with high PD-L1 expression have shown potentially better efficacy results than subjects with low PD-L1 expression. Seven out of the 20 evaluable NPC subjects had high PD-L1 expression, of which five subjects had PRs, and the DCR and ORR was 85.7% and 71.4%, respectively. All the seven subjects were anti-PD-(L)1 treatment naïve. Among the other 13 evaluable NPC subjects with low PD-L1 expression, the DCR was 46.2%. It is believed that higher dose levels would be required for subjects with low PD-L1 expression to achieve better response and disease control.

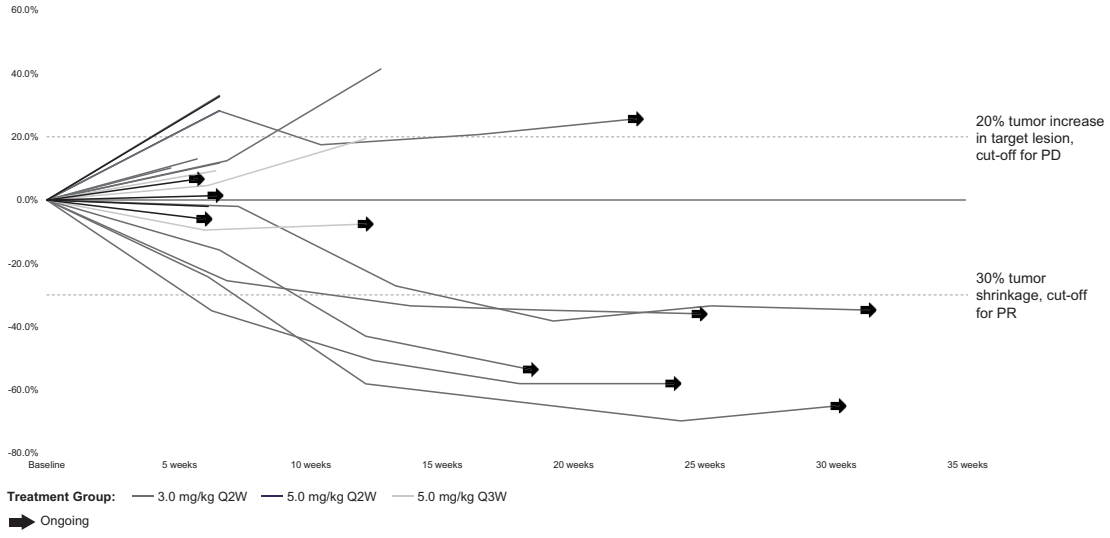
All the 20 evaluable NPC subjects received KN046 at 3.0 mg/kg or higher dose levels Q2W/Q3W, and nine had a treatment duration of at least 12 weeks. Among the nine subjects, five had confirmed PRs and two had SD. The following swimming lane graph illustrates the treatment duration and the best overall responses of the 20 evaluable NPC subjects as of the Data Cut-off Date.



Abbreviations: PR = partial response, SD = stable disease, PD = progressive disease, uPR = unconfirmed partial response, NPC = nasopharyngeal cancer.

Source: Internal clinical trial data

The following spider plot shows the change of target lesions across treatment duration of the 20 evaluable NPC subjects as of the Data Cut-off Date.



Source: Internal clinical trial data

PK profile. PK studies following the first 90 minutes of infusion and dose proportionality of KN046 have been characterized in 58 subjects in the phase Ia clinical trial. Average half-life of KN046 in the 5.0 mg/kg Q2W cohort was approximately seven days. The preliminary concentrations obtained over time and the drug clearance during the first dosing interval appear to be similar in the dose escalation study of KN046-CHN-001 trial and the KN046-AUS-001 trial.

Conclusion. KN046 showed a favorable safety profile and promising preliminary anti-tumor efficacy results especially in NPC subjects. KN046 is not sensitive to ethnic factors in terms of drug safety, tolerability and PK, as observed in the KN046-CHN-001 trial and the dose escalation study of the KN046-AUS-001 trial.

Phase II Clinical Trials

Phase II Clinical Trial for NSCLC in China (KN046-201)

KN046-201 is an on-going multi-center, open-label, single-arm phase II clinical trial in China of KN046 as a second-line or later-line monotherapy or a part of combination therapies with TKIs in patients with locally advanced unresectable or metastatic NSCLC and without EGFR or ALK mutations. As of the Data Cut-off Date, 23 subjects were enrolled in this trial and 22 subjects had received at least one dose of KN046 per treatment.

Study purpose. The primary objective of KN046-201 is to evaluate anti-tumor activities of KN046 and the secondary objectives are safety and tolerability of KN046. The primary endpoints are ORR and DOR assessed according to RECIST version 1.1. The secondary endpoints primarily include TEAEs, PK parameters, ADAs, and association of biomarkers and efficacy parameters.

Study design. KN046-201 trial designed four cohorts, which would be carried in sequence. The first two cohorts would recruit subjects who failed first-line chemotherapy and treatment naïve in PD-(L)1 inhibitors, and subjects in these cohorts would receive KN046 as a monotherapy at 3.0 mg/kg Q2W and 5.0 mg/kg Q2W, respectively. The third cohort would recruit subjects who have failed first-line chemotherapy and refractory or resistant to prior line of PD-(L)1 inhibitors. The last cohort would recruit subjects with EGFR mutant NSCLC. Dose regimen and schedule of KN046 of the last two cohorts would be determined based on the safety and efficacy results from the first two cohorts in addition to data from other KN046 studies. Safety and tolerability would be primarily assessed by monitoring TEAEs. Tumor assessments would be performed according to RECIST version 1.1.

Safety. As of the Data Cut-off Date, all 22 subjects enrolled in KN046-201 trial were included in the safety data analysis, of which 20 subjects remained on the study treatment and two subjects discontinued treatment due to poor patient compliance and disease progression. All the subjects were enrolled in the 3.0 mg/kg Q2W cohort. The results have exhibited favourable safety and tolerability profile and are consistent with the safety profile observed in the phase I clinical trials. The median duration of the exposure of KN046 was approximately eight weeks, ranging from two to 19 weeks.

As of the Data Cut-off Date, 16 (72.7%) out of the 22 subjects had experienced treatment-related TEAE of all grades and two (9.1%) had experienced treatment-related TEAEs at grade 3 or higher levels. Four (18.2%) subjects experienced treatment-related SAEs. Seven (31.8%) subjects had experienced irAEs, none of which was grade 3. Details of the TEAEs observed from all the 22 subjects are summarized in the following table.

TEAE categories[1]	Total (N=22)
	n (%)
All TEAEs	19 (86.4%)
TEAE, Grade ≥3	2 (9.1%)
Treatment-related TEAEs [2]	16 (72.7%)
Treatment-related TEAEs, Grade ≥3 [3]	2 (9.1%)
SAEs	5 (22.7%)
Treatment-related SAEs [4]	4 (18.2%)
IrAEs[5]	7 (31.8%)
IrAEs, Grade ≥3	0
TEAEs leading to permanent treatment discontinuation	1 (4.5%)
Treatment-related TEAEs leading to permanent treatment discontinuation	0
Treatment-related TEAE leading to death	0

(1) Reported under National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.

(2) The most frequent treatment-related TEAEs (n≥2) included infusion-related reaction (n=3, 13.6%), fever (n=2, 9.1%), asthenia (n=3, 13.6%), hepatic function abnormal (n=2, 9.1%), hyperglycemia (n=2, 9.1%), joint pain (n=2, 9.1%), anemia (n=3, 13.6%), alanine aminotransferase increased (n=2, 9.1%) and rash (n=2, 9.1%).

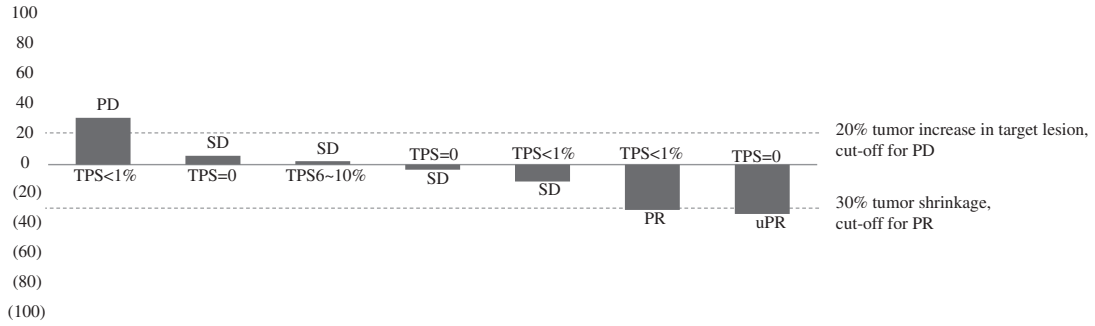
(3) Including pulmonary infection (n=1, 4.5%) and lymphangitis (n=1, 4.5%).

(4) Including asthenia (n=1, 4.5%), autoimmune hepatitis (n=1, 4.5%), pulmonary infection (n=1, 4.5%) and lymphangitis (n=1, 4.5%).

(5) Seven subjects experienced nine irAEs, including fever (n=1, 4.5%), joint pain (n=1, 4.5%), muscular tension (n=1, 4.5%), hyperthyroidism (n=1, 4.5%), mastication disorder (n=1, 4.5%), facial pain (n=1, 4.5%), rash (n=2, 9.1%), autoimmune hepatitis (n=1, 4.5%).

Efficacy. All the subjects were enrolled in the 3.0 mg/kg Q2W cohort. As of the Data Cut-off Date, there were seven evaluable subjects. The preliminary efficacy results showed that among the seven evaluable subjects, one had a confirmed PR, one had an unconfirmed PR and four had SD. The DCR was 85.7% and the ORR was 28.6% as of the same date. The following waterfall plot shows the best overall response of the seven evaluable subjects receiving KN046 at 3.0 mg/kg Q2W as measured by percentage of change of target lesions from baseline based on CT/MRI scans.

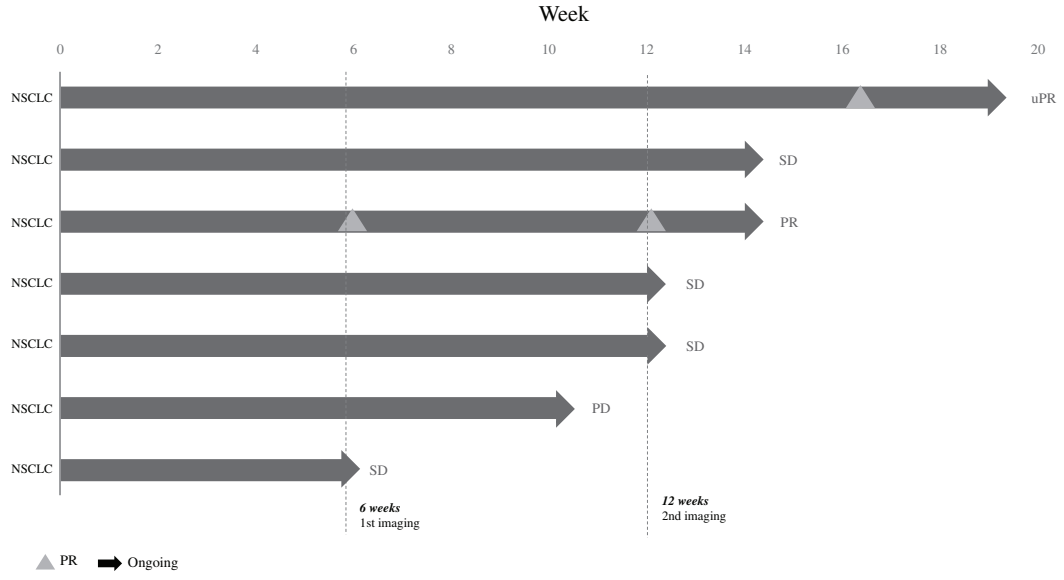
Tumor Target Lesion Shrinkage from Baseline (%)



Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response, TPS=tumor proportion score.

Source: Internal clinical trial data

As of the Data Cut-off Date, all the seven evaluable NSCLC subjects remained on treatment, and five subjects had a treatment duration of at least 12 weeks. The following swimming lane graph illustrates the treatment duration and the best overall responses of the seven evaluable NSCLC subjects as of the Data Cut-off Date.



Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response.

Source: Internal clinical trial data

Conclusion. In NSCLC subjects, our KN046 exhibited favorable safety profile and preliminary efficacy results, indicating promising anti-tumor activities.

Phase Ib/II Clinical Trial for TNBC in China (KN046-203)

KN046-203 is an on-going multi-center, open-label, single arm phase Ib/II clinical trial in China of KN046 as a first-line therapy combined with chemotherapy or second-line monotherapy in patients with locally advanced or metastatic TNBC. As of the Data Cut-off Date, 18 subjects were enrolled in this trial and had received at least one dose of KN046 per treatment.

Study design. KN046-203 trial consisted two parts, one second-line monotherapy evaluation and one first-line combination therapy evaluation. For the second-line monotherapy evaluation, subjects who have failed at least one prior line of systemic chemotherapy would be enrolled across two cohorts of 3 mg/kg Q2W and 5 mg/kg Q2W. For KN046 in the combination therapy evaluation, subjects who are systemic treatment naïve would be enrolled across two cohorts of 3 mg/kg Q2W and 5 mg/kg Q2W. Safety and tolerability would be primarily assessed by monitoring TEAEs. Tumor assessments would be performed according to RECIST version 1.1.

Safety. As of the Data Cut-off Date, all 18 subjects enrolled in KN046-203 trial were included in the safety data analysis, including 14 subjects enrolled in the monotherapy evaluation (nine in the 3 mg/kg Q2W cohort and five in the 5 mg/kg Q2W cohort) and four enrolled in the 3 mg/kg Q2W cohort of the combination therapy evaluation. The results have exhibited favourable safety and tolerability profile and are consistent with the safety profile observed in the phase I clinical trials. The median duration of the exposure of KN046 was five weeks, ranging from two to 14 weeks.

As of the Data Cut-off Date, nine (50%) out of the 18 subjects had experienced treatment-related TEAE of all grades and three (16.7%) had experienced treatment-related TEAEs at grade 3 or higher levels. Two (11.1%) subjects experienced treatment-related SAEs. One (5.6%) subject had experienced a grade 2 irAE. Details of the TEAEs observed from all the 18 subjects are summarized in the following table.

TEAE categories[(1)]	**Total (N=18)**
	n (%)
All TEAEs	10 (55.6%)
TEAE, Grade ≥3	5 (27.8%)
Treatment-related TEAEs[(2)]	9 (50%)
Treatment-related TEAEs, Grade ≥3[(3)]	3 (16.7%)

TEAE categories[1]	Total (N=18)
SAEs	3 (16.7%)
Treatment-related SAEs[4]	2 (11.1%)
SAEs, Grade ≥3	2 (11.1%)
Treatment-related SAEs, Grade ≥3	1 (5.6%)
IrAE[5]	1 (5.6%)
IrAE, Grade ≥3	0
TEAEs leading to permanent treatment discontinuation	2 (11.1%)
Treatment-related TEAEs leading to permanent treatment discontinuation	0
Treatment-related TEAE leading to death	0

(1) Reported under National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0.

(2) The most frequent treatment-related TEAEs (n≥2) included aspartate aminotransferase increased and diarrhea (each n=3, 16.7%), white blood cell count decreased, pyrexia, chills, vomiting, alopecia, thrombocyte count decreased and absolute neutrophil count decreased (each n=2, 11.1%).

(3) Three subjects experienced seven treatment-related TEAEs at grade 3 or higher levels, including white blood cell count decreased, aspartate aminotransferase increased, absolute neutrophil count decreased, hypokalemia, fatigue and confusional state (each n=1, 5.6%).

(4) Including thrombocyte count decreased, infusion related reaction and confusional state (each n=1, 5.6%).

(5) Including one thrombocyte count decreased.

Source: Internal clinical trial data

Efficacy. As of the Data Cut-off Date, the monotherapy group had five evaluable subjects, of which two had SD and the DCR was 40.0%. As of the same date, the combination therapy group had three evaluable subjects with treatment ongoing, of which two had unconfirmed PR (one had 100% reduction of target lesion from baseline after the first assessment and a treatment duration of approximately 10.4 weeks, and the other had 51% reduction of target lesion from baseline after the first assessment and a treatment duration of approximately 10 weeks) and one had SD (with 23 % reduction of target lesion from baseline after the first assessment and a treatment duration of approximately 11.9 weeks). All the three evaluable subjects in the combination therapy group achieved disease control and the ORR was 66.7% as of the same date.

Conclusion. In TNBC subjects, our KN046 exhibited favorable safety profile and preliminary efficacy results, indicating promising anti-tumor activities.

Clinical Trial Development Plan

We are executing a comprehensive clinical trial development plan in China, Australia and the United States targeting an array of cancer indications for our KN046, including as a monotherapy and in combination with other therapies, with the purpose of supporting registration of KN046 for multiple indications in China and the United States. The table below sets forth details of the clinical development plan of our KN046.

Trial No.	Indication	Clinical trial stage	Type of therapy	Primary objectives /endpoints	Secondary objectives/ endpoints	Planned size	(Expected) trial initiation date[1]	Expected trial completion date[2]	Expected BLA submission date	Status	Location and competent authority	Current standard of care
KN046-AUS-001[3]	Metastatic or locally advanced solid tumors	Phase I	Mono	Determine the MTD or BED and/or RP2D	Evaluate preliminary anti-tumor activities and to characterize PK profile	~ 45	June 2018	February 2020	Not applicable	Phase Ia completed, phase Ib ongoing	Australia/ TGA	Not applicable
KN046-CHN-001(a)[4]	Solid tumors or hematological malignancies	Dose escalation	Mono	Determine the MTD and/or RP2D	Evaluate the preliminary anti-tumor activities and to characterize PK profile	~ 55	December, 2018	July 2019	Not applicable	Ongoing	China/ NMPA	Not applicable
KN046-CHN-001(b)[4]	≥3L unresectable/ metastatic NPC[4]	Dose expansion	Mono	Best overall response (BOR) and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters; anti-drug antibodies (ADAs); association of biomarker and efficacy parameters	~ 100	3Q 2019	1Q 2021	3Q 2021	Planning stage	China/ NMPA	Not available
	≥2L unresectable/ metastatic UC[4]					~ 30	1Q 2020	3Q 2021	1Q 2022			Not available
	≥ 2L unresectable/ metastatic melanoma[4]					~ 30	1Q 2020	3Q 2021	1Q 2022			Pembrolizumab and JS001
	≥2L extensive stage SCLC					~ 30 to 60	1Q 2020	3Q 2021	1Q 2022			Topotecan

Trial No.	Indication	Clinical trial stage	Type of therapy	Primary objectives /endpoints	Secondary objectives/ endpoints	Planned size	(Expected) trial initiation date[1]	Expected trial completion date[2]	Expected BLA submission date	Status	Location and competent authority	Current standard of care
KN046-201[5]	≥2L locally advanced unresectable or metastatic NSCLC excluding EGFR/ALK mutation (anti-PD-(L)1 treatment naïve or refractory)	Phase II	Mono or Combo (with multi-TKI)	ORR and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters, ADAs, association of biomarker and efficacy parameters	~60 to up to ~160	May 2019	3Q 2020	1Q 2023	Ongoing	China/ NMPA(US/FDA if expanded into a global trial)	Chemo or PD-1 inhibitors alone
KN046-202[6]	1L locally advanced unresectable or metastatic NSCLC excluding EGFR/ALK mutation	Phase II	Combo (with chemo)	ORR and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters, ADAs, association of biomarker and efficacy parameters	~50	September 2019	2Q 2020	1Q 2023	Ongoing	China/NMPA	Chemo in combination with PD-(L)1 inhibitors
KN046-203[7]	1L locally advanced or metastatic TNBC	Phase Ib/II	Combo (with chemo or chemo plus VEGFR)	ORR and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters, ADAs, association of biomarker and efficacy parameters	~50	May 2019	3Q 2020	1Q 2023	Ongoing	China/NMPA	Chemo
	2L locally advanced or metastatic TNBC		Mono			~60						
KN046-204[8]	2L locally advanced/recurrent or metastatic ESCC	Phase II	Mono	ORR and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters, ADAs, association of biomarker and efficacy parameters	~30	May 2019	3Q 2020	1Q 2023	Ongoing	China/NMPA	Not available

Trial No.	Indication	Clinical trial stage	Type of therapy	Primary objectives /endpoints	Secondary objectives/ endpoints	Planned size	(Expected) trial initiation date[1]	Expected trial completion date[2]	Expected BLA submission date	Status	Location and competent authority	Current standard of care
KN046-205[9]	≥2L pancreatic cancer	Phase II	Mono	ORR and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters, ADAs, association of biomarker and efficacy parameters	25	1Q 2020	3Q 2021	Not applicable	Planning stage	China/NMPA	Chemo
KN046-210[10]	≥2L locally advanced unresectable or metastatic soft tissue sarcoma[10]	Exploratory trial	Mono	ORR and DOR according to RECIST 1.1	Evaluate CBR, DCR, PFS and overall survival rates at 6 months and 12 months, TEAEs by CTCAE v5.0, PK parameters	Planning stage	4Q 2020	3Q 2022	4Q 2022	Planning stage	China/ NMPA	Chemo and TKI

Abbreviations: 1L = first-line, 2L = second-line, mono = monotherapy, combo = combination therapy, chemo = chemotherapy, NPC = nasopharyngeal cancer, UC = urothelial carcinoma, TNBC = triple negative breast cancer; VEGFR = vascular endothelial growth factor receptor, NSCLC = non-small cell lung cancer, TKI = tyrosine-kinase inhibitors, ESCC = esophageal squamous cell carcinoma, EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma kinase.

* We also use immune response criteria in solid tumors (iRECIST) to (i) assess immune-related iORR, iDCR and iPFS as exploratory efficacy endpoints in addition to primary and secondary efficacy endpoints; and (ii) allow response categories of both confirmed PD and unconfirmed PD and provide treatment guidance for post initial RECIST 1.1-based PD.

(1) Denotes the date on which first patient was enrolled.

(2) Denotes the date on which the last visit was made by the last patient.

(3) A multi-center, open-label, single arm clinical trial.

(4) Two parts of KN046-CHN-001 trial, a multi-center, open-label, single arm clinical trial.

(5) A multi-center, open-label, single arm clinical trial. If the data from this trial is positive, we may initiate a phase III clinical for this indication and expand the trial into the United States to form a global trial, subject to receiving IND approval from the FDA.

(6) A multi-center, open-label, single arm clinical trial. If the data from this trial is positive, we may initiate a phase III clinical for this indication and expand the trial into the United States to form a global trial, subject to receiving IND approval from the FDA. As of the Latest Practicable Date, we enrolled 21 subjects in this trial.

(7) A multi-center, open-label, single arm clinical trial. If the data from this trial is positive, we may initiate a phase III clinical for this indication and expand the trial into the United States to form a global trial, subject to receiving IND approval from the FDA.

(8) A multi-center, open-label, single arm trial. If the data from this trial is positive, we may initiate a phase III clinical for this indication and expand the trial into the United States to form a global trial, subject to receiving IND approval from the FDA. As of the Latest Practicable Date, we enrolled 17 subjects in this trial.

(9) A multi-center, open-label, single arm clinical trial.

(10) We plan to conduct an exploratory clinical trial for at most six subtypes of soft tissue sarcoma, namely, undifferentiated pleomorphic sarcoma, liposarcoma, alveolar soft part sarcoma, leiomyosarcoma, Kaposi's sarcoma and chondrosarcoma.

We are conducting the KN046-AUS-001 trial and the dose escalation study of the KN046-CHN-001 trial for solid tumors or hematological malignancies primarily to assess the safety and determine the RP2D for the following trials. For preliminary clinical results, see "—Summary of Clinical Results—Phase I Clinical Trials—Phase I Clinical Trial in Australia (KN046-AUS-001)" and "—Summary of Clinical Results—Phase I Clinical Trials—Phase I Clinical Trial in China (KN046-CHN-001)."

Indications Under Fast/First-to-Market Approach

Under a fast/first-to-market approach, during the dose expansion phase of the KN046-CHN-001 trial, we plan to strategically focus on late-line unresectable/metastatic NPC, urothelial cancer and melanoma. Although these indications have relatively low cancer incidences and represent a smaller fraction of the total cancer population in China compared to major cancer indications, according to the CIC Report, late-line patients with these indications have limited choices of existing therapies, which allows us to conduct single arm registration trial(s) with much smaller patient sizes compared to major indications. We plan to advance the trials for third-line or later-line NPC first, considering the early efficacy signals observed in the KN046-CHN-001 trial and no PD-(L)1 inhibitors were approved for such indication. See "—Summary of Clinical Results—Phase I Clinical Trials—Phase I Clinical Trial in China (KN046-CHN-001)—Efficacy." We expect to file the first BLA for KN046 with NMPA in 2021 for this indication.

Major Indications

To explore the market potential of our KN046, we are strategically developing KN046 for several major cancer indications, including late stage NSCLC, TNBC, ESCC and pancreatic cancer.

- *Locally advanced unresectable or metastatic NSCLC*. Lung cancer has the largest cancer incidence in China and is expected to remain the most prevalent type of cancer in the next decade. NSCLC accounts for approximately 80% to 85% of the lung cancer population. Among NSCLC patients, approximately 80% are diagnosed with locally advanced unresectable or metastatic NSCLC. In China and the United States, currently the first-line standard of care for NSCLC is chemotherapy in combination with PD-(L)1 inhibitors and the second-line standard of care is chemotherapy or PD-1 inhibitors alone. Although immune checkpoint inhibitors have significantly improved the overall survival rate of NSCLC patients form approximately 5% to 20%, there are still existing significant unmet needs.

- *Locally advanced or metastatic TNBC*. Breast cancer is one of the most common cancer types in China. When the breast cancer patients are first diagnosed, approximately 15% to 20% are determined to be TNBC in China. The current standard of care for TNBC is chemotherapy and the five-year overall survival rate is approximately 58% for early-stage TNBC and only 10 months for locally advanced unresectable or metastatic TNBC.

- *Advanced/Recurrent or metastatic ESCC*. Over 90% of esophageal cancer patients are pathologically diagnosed as ESCC, and a majority of patients do not survive due to recurrence with a five-year survival rate from approximately 15% to 25%.

- *Pancreatic cancer*. Pancreatic cancer is one of most common cancers in China and is considered as one of the most malignant tumors worldwide. Its total five-year survival rate is still less than 8% regardless of combination with chemotherapy and radiotherapy.

Combination with KN026

We plan to conduct clinical trials on GC/GEJ, urothelial cancer and ovarian cancer through combination therapies of our KN046 and KN026, which we believe have potential to improve response rate and maximize the market value of our pipeline products. See "—Anti-HER2 BsAb Candidate – KN026—Clinical Trial Development Plan."

Indications with Unmet Medical Needs

Soft tissue sarcoma has various subtypes. Metastatic lesions can be detected in approximately 10% of patients with soft tissue sarcoma at the time of diagnosis. Furthermore, 25% of patients with sarcomas develop metastatic disease after curative treatment for the primary tumor.

Competition

To date, there are no approved BsAbs targeting PD-(L)1 and CTLA-4 on the market. As of August 31, 2019, there were six BsAb candidates in total targeting two different immune checkpoints in clinical trials or later stage in China and the United States. Currently a majority of approved and clinical-stage immune checkpoint inhibitors against PD-1, PD-L1 and CTLA-4 are monospecific antibodies, studies of the combination therapies have shown the dual blockade of both PD-(L)1 and CTLA-4 checkpoints can induce stronger anti-tumor responses in certain types of cancers than a single blockade of each agent. This indicates a potentially better efficacy of anti-PD-(L)1/CTLA-4 BsAbs than the monospecific inhibitor in certain cancer indications. The only approved therapy to induce dual blockade of PD-(L)1 and CTLA-4 is the combination therapy of Opdivo and Yervoy, which has not been approved in China. See "—Current Therapy and Limitations" and "Industry Overview—Overview of the Immune Checkpoint Inhibitor Market in the PRC and United States". In addition, as of August 31, 2019, there were two and four anti-PD-(L)1/CTLA-4 combination therapy candidates in China and the United States in phase III clinical trials or later stage, respectively. The following table sets forth details of major drug candidates that may compete with our KN046 as of August 31, 2019.

Anti-PD-(L)1/CTLA-4 BsAb Candidates

Drug candidate name	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date
PRC					
KN046	Alphamab	PD-L1/CTLA-4	NSCLC	Phase II	Jan-2019
				Phase II (with chemo)	Jun-2019
			ESCC	Phase II	May-2019
			TNBC	Phase Ib/II (with chemo)	Apr-2019
			Solid tumors	Phase I	Nov-2018
AK104	Akeso Biopharma, Inc.	PD-1/CTLA-4	Solid tumors	Phase Ib/II	Dec-2018
			GC/GEJ	Phase Ib/II (with chemo)	Dec-2018
IBI-318	Innovent	PD-1/PD-L1	Malignant neoplasm	Phase I	Mar-2019
U.S.					
MEDI5752	AstraZeneca	PD-1/CTLA-4	Solid tumors	Phase I (mono or with chemo)	May-2018
XmAb20717	Xencor, Inc.	PD-1/CTLA-4	Solid tumors	Phase I	May-2018
MGD019	MacroGenics, Inc.	PD-1/CTLA-4	Solid tumors	Phase I	Dec-2018

Combination Therapy Candidates of PD-(L)1 and CTLA-4 Inhibitors (Phase III or Later Stage)

Drug candidate name	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date
PRC					
Nivolumab/ Ipilimumab	BMS	PD-1/CTLA-4	GC/GEJ	Phase III	May-2017
			SCLC	Phase III	Jul-2017
			Pleural mesothelioma	Phase III	Sep-2017
			ESCC	Phase III	Feb-2018
			RCC	Phase III	Mar-2018
			UC	Phase III	Jun-2018
			NSCLC	Phase III	Apr-2017
Durvalumab/ Tremelimumab	AstraZeneca/ MedImmune	PD-L1/CTLA-4	NSCLC	Phase III	Jan-2017
			SCLC	Phase III	May-2018
			HCC	Phase III	Jun-2018
U.S.					
Nivolumab/ Ipilimumab	BMS	PD-1/CTLA-4	Glioblastoma	Phase III	Jan-2014
			RCC	Phase III	Oct-2014
			Melanoma	Phase III	Mar-2015
			NSCLC	Phase III	Aug-2015
			HNSCC	Phase III	Aug-2016
			GC/GEJ	Phase III	Oct-2016
			Pleural mesothelioma	Phase III	Oct-2016
			UC	Phase III	Mar-2017
			Esophageal cancer	Phase III	Jun-2017
			CRC	Phase III	Jul-2019

Drug candidate name	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date
Durvalumab/ Tremelimumab	AstraZeneca/ MedImmune	PD-L1/CTLA-4	NSCLC	Phase III	Jan-2015
			HNSCC	Phase III	Sep-2015
			UC	Phase III	Nov-2015
			SCLC	Phase III	Mar-2017
			Solid tumors	Phase III	Apr-2017
			HCC	Phase III	Oct-2017
Pembrolizumab/ Ipilimumab	Merck	PD-1/CTLA-4	NSCLC	Phase III	Dec-2017
Cemiplimab/ Ipilimumab	Regeneron Pharmaceuticals, Inc./ Sanofi S.A.	PD-1/CTLA-4	NSCLC	Phase III	Mar-2018

Abbreviations: NSCLC = non-small cell lung cancer, SCLC = small cell lung cancer, ESCC = esophageal squamous cell carcinoma, TNBC = triple negative breast cancer, GC = gastric cancer, GEJ = gastroesophageal junction cancer, UC = urothelial cancer, RCC = renal cell carcinoma, HNSCC = head and neck squamous-cell carcinoma, HCC = hepatocellular carcinoma, NSCLC = non-small cell lung cancer.

Source: NMPA;FDA;CIC Report (As of August 31, 2019)

Compared with the approved combination therapy and combination therapy candidates with ipilimumab as a component, our KN046 has a potentially favorable safety profile and a broad therapeutic window, which could allow a higher and longer drug exposure. Certain combination therapy candidates select tremelimumab, an IgG2 anti-CTLA-4 antibody, which has a weakened Fc effector function profile compared with an IgG1 antibody such as our KN046. Our KN046 is the only anti-PD-L1/CTLA-4 BsAb candidate and the only anti-PD-(L)1 and CTLA-4 BsAb candidate with multiple indications in phase II clinical trials. In addition to pursuing major cancer indications with a larger patient population size in China similar to competing BsAb and combination therapy candidates, we have also selected certain small indications with relatively lower cancer incidences and representing a smaller fraction of the total cancer population in China as compared to major cancer indications.

Material Communications and Next Steps

In March 2018, Alphamab Australia received an IND approval from the TGA for the initiation of clinical trials for KN046 in Australia. In July 2018, Jiangsu Alphamab received an Umbrella IND approval from the NMPA for the initiation of clinical trials for our KN046 in China. We have consulted with the CDE of the NMPA on the safety study and dosage design of our phase Ia clinical trial, the preliminary safety and PK data of our phase Ia clinical trial, and the efficacy study and dosage design of our phase II clinical trial. The CDE expressed no concerns on the preliminary clinical results of our phase Ia trials. We have not received objections to the commencement of our phase II clinical trials as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET KN046 SUCCESSFULLY.

Anti-HER2 BsAb Candidate – KN026

Overview

Our KN026 is a BsAb that targets two different domains of HER2. Overexpression of HER2 has been observed to be a key factor in tumor formation and progression, including breast cancer. Currently, there are no approved anti-HER2 BsAbs worldwide. The only approved therapy with dual HER2 signal blockade is Roche's Herceptin (trastuzumab) in combination with Roche's Perjeta (pertuzumab) and chemotherapy. Although such combination therapy demonstrated efficacy for HER2 High cancers, it covers limited cancer indications and is ineffective against HER2 Low and HER2 Intermediate cancers.

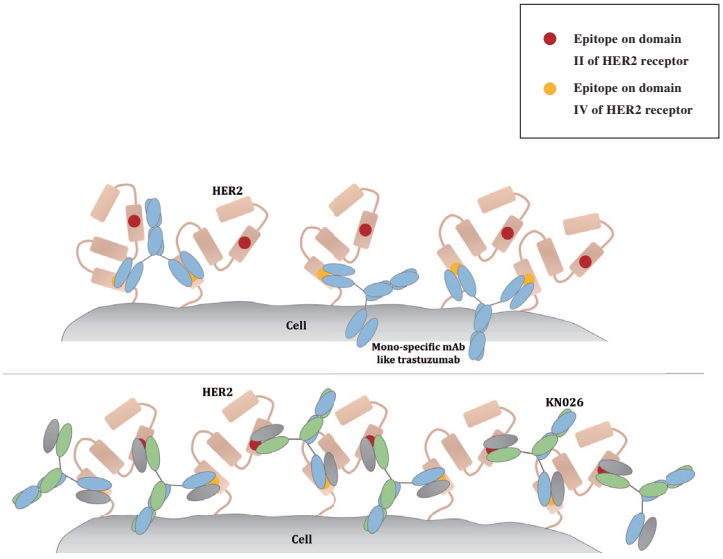
We received an Umbrella IND approval from the NMPA in March 2018 and an IND approval from the FDA in October 2018 for our KN026. We are currently conducting a phase I clinical trial in China on HER2 High breast cancer or GC/GEJ. We are also conducting a phase II clinical trial for second-line HER2-overexpressing GC/GEJ in China and a phase I clinical trial for HER2-overexpressing solid tumors, including but not limited to breast cancer and GC/GEJ, in the United States. We plan to conduct a number of clinical trials for different cancer indications with KN026 in 2019 and 2020. See "—Clinical Trial Development Plan."

Mechanism of Action

HER2 is a member of the human epidermal growth factor receptor (HER) family. The HER family interacts with a number of signaling molecules and promotes cell proliferation. Dimerization of the HER2 receptor initiates a variety of signaling pathways, leading to excessive uncontrolled cell growth and tumorigenesis. KN026 inhibits HER2 expression through the following mechanisms:

- *Dual blockade of parallel HER2-related signaling pathways*. KN026 binds two distinct epitopes of HER2 receptors which have been clinically validated by the Herceptin and Perjeta combination therapy. Such binding results in a dual blockade of two different and complementary HER2-related signaling pathways, which we believe can induce synergistic inhibition activities against HER2 overexpression and potentially reduce drug resistance and relapse;

- *Enhanced multiple HER2 receptor binding*. Binding of bispecific antibodies can connect multiple HER2 receptors on the cell surface and promote HER2 receptor clustering, which can (i) strengthen binding to HER2 receptors, which translates to stronger inhibition; (ii) induce internalization of HER2 receptors to reduce HER2 proteins on the cell surface, leading to reduced HER2 signaling; and (iii) increase presence of antibodies on the surface of tumor cells. The following diagram illustrates the difference in HER2 binding activities of monospecific anti-HER2 antibodies and our KN026 due to HER2 clustering;



* Our KN026 binds both domain II and domain IV of HER2 receptors, and monospecific antibodies such as trastuzumab or pertuzumab only bind domain IV or domain II of HER2 receptors, respectively. In comparing the binding mode of KN026 and monospecific antibodies, it has been shown that (i) more KN026 are bound to the cell surface with the same intensity of HER2 receptors; (ii) KN026 can connect HER2 receptors together to form clusters.

- *Fc-based BsAb with full effector functions*. Our KN026 preserves the full Fc-mediated effector functions, which is critical to recruiting immune cells to destroy HER2-overexpressing target cells. In addition, the increased presence of KN026 on tumor cells leads to increased tumor killing by effector functions.

We believe the combination of these mechanisms enables our KN026 to be a potential next-generation HER2-targeted therapy, due to the potential advantages exhibited in pre-clinical and clinical studies. See "—Anti-HER2 BsAb Candidate – KN026—Potential Advantages of KN026" below.

Current Anti-HER2 Antibody Drugs and Limitations

To date, there are no approved anti-HER2 BsAbs worldwide. There are three approved anti-HER2 antibody drugs on the global market, including two monospecific antibodies, namely, trastuzumab (sold primarily under the trade name Herceptin) and pertuzumab (sold under the trade name Perjeta and only approved in combination usage with trastuzumab), and an ADC that attaches trastuzumab with a chemical linker to the chemotherapy DM1, namely, T-DM1 (sold under the trade name Kadcyla), according to the CIC Report. With respect to the ADC, however, the small molecule toxin in such ADC differentiates its safety profile from other antibody drugs and therefore we do not consider it as a potential competitor for KN026. All of these therapies are approved in the United States, and trastuzumab and pertuzumab are approved in China.

Trastuzumab is the only antibody approved for combination and/or standalone treatments and the only approved antibody globally for HER2 High breast cancer and for HER2 High metastatic GC/GEJ. It has been a global top-selling oncology drug for decades. Pertuzumab is approved (i) as a part of a combination therapy with trastuzumab plus chemotherapy for HER2 High metastatic breast cancer, or (ii) as neoadjuvant/adjuvant treatments for HER2 High early breast cancer in the United States, of which only the adjuvant treatment is approved in China. Such combination therapies successfully verify the dual blockade mechanism of trastuzumab and pertuzumab and have demonstrated improved treatment efficacy over trastuzumab as a monotherapy. With superior efficacy over trastuzumab, the combination therapy of trastuzumab, pertuzumab and chemotherapy using docetaxel has become the first-line standard-of-care treatment for HER2 High metastatic breast cancer in the United States. In a phase III trial of trastuzumab (NCT:00567190), the combination of trastuzumab, pertuzumab and chemotherapy using docetaxel results in an average overall survival benefit of 56.5 months, a PFS of 18.5 months and an ORR of 80.2%, which is better than the overall survival benefit of 40.8 months, PFS of 12.4 months and ORR of 69.3% induced by trastuzumab plus chemotherapy. After the advent of these two antibody drugs, the treatment efficacy in patients with breast cancer and metastatic GC/GEJ, especially their overall survival benefit, improved significantly.

Despite the clinical benefits achieved by current antibody drugs, they are only approved for HER2 High breast cancer and metastatic GC/GEJ, and are not approved for a number of other major cancer indications closely associated with HER2 High overexpression, such as colorectal cancer, urothelial cancer, ovarian cancer and gallbladder cancer. In addition, approximately 66% of breast cancer and over 24% of GC/GEJ express low to intermediate levels of HER2, and it is believed that other cancer types also express HER2 at varying levels, including low to intermediate levels. All of these HER2 Low or Intermediate cancer patients are ineligible for current anti-HER2 antibody therapies and these patients could potentially benefit from our KN026.

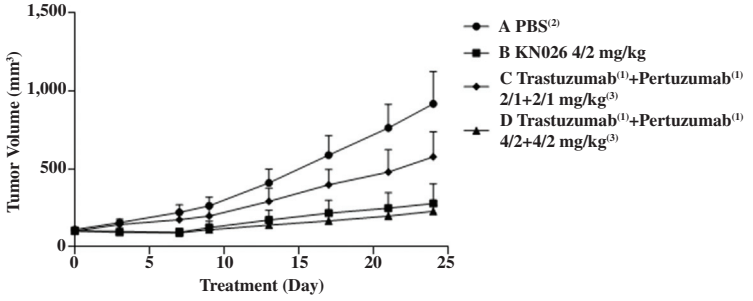
Potential Advantages of KN026

Compared with current anti-HER2 antibody drugs, we believe our KN026 has the following potential advantages, as observed in our clinical and pre-clinical studies:

- *Efficacy for HER2 High breast cancer that failed prior HER2-targeted treatment(s).* According to the preliminary efficacy results of the phase I clinical study in China, KN026 had shown a meaningful clinical benefit in breast cancer patients who had received at least one prior HER2-targeted treatment. As of September 20, 2019, the data cut-off date of our phase I clinical study, we had six PRs (one confirmed and five unconfirmed) who had previously received one to four lines of HER2-targeted treatments, five SD subjects who had previously received one to two lines of HER2-targeted treatments, and four SD subjects who had previously been heavily treated with three to six lines of HER2-targeted treatments, indicating that our KN026 has efficacy for patients with HER2 High breast cancer after numerous prior treatments, including trastuzumab, two targeted small molecule drugs, namely lapatinib and pyrotinib, and an investigational ADC drug candidate. See "—Summary of Clinical Results—Phase I Clinical Trial in China (KN026-CHN-001)—Efficacy." Our pre-clinical studies also exhibited efficacy of KN026 against a trastuzumab-resistant cancer cell line.

- *Better potency than trastuzumab plus pertuzumab against HER2 High cancers*

  - *In vivo studies against HER2 High NSCLC.* In *in vivo* studies of each of KN026 and the trastuzumab plus pertuzumab combination in human HER2 High NSCLC Calu-3 cells transplanted in mice, the results showed that KN026 induced (i) a higher tumor growth inhibitory rate at a 4.0/2.0 mg/kg dose level than the trastuzumab plus pertuzumab combination at an equal drug concentration in terms of total molar mass (trastuzumab at 2.0/1.0 mg/kg and pertuzumab at 2.0/1.0 mg/kg); and (ii) a comparable tumor growth inhibitory rate at a 4.0/2.0 mg/kg dose level than the combination at a two-fold higher dose level in terms of total molar mass (trastuzumab at 4.0/2.0 mg/kg and pertuzumab at 4.0/2.0 mg/kg). See "—Pre-clinical Studies—Xenograft Tumor Model against HER2 High Cell Line." The following graph illustrates tumor volume changes after injection of KN026, and trastuzumab plus pertuzumab combination in the NSCLC cell line.



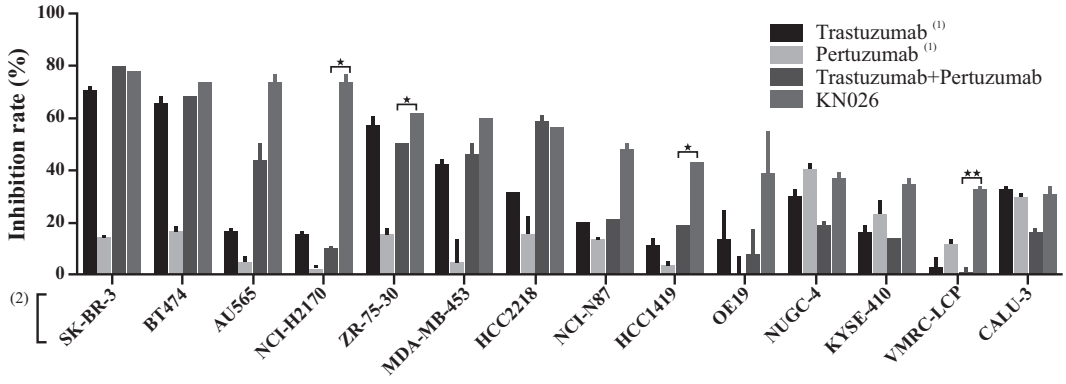
(1) Trastuzumab was Herceptin purchased from Roche. Pertuzumab was a biosimilar to Perjeta produced by us in-house.

(2) The group receiving PBS was a negative control group.

(3) The trastuzumab plus pertuzumab combination was given at two dose levels, including (i) 2.0/1.0 mg/kg and 2.0/1.0 mg/kg (equal to KN026 at 4.0/2.0 mg/kg in terms of total molar mass); and (ii) 4.0/2.0 mg/kg and 4.0/2.0 mg/kg (a two-fold higher dose level than KN026 at 4.0/2.0 mg/kg in terms of total molar mass). The first number of each dose level is the first dosage amount and the second number of each dose level is the maintenance dosage amount after the first dose. The first dosage doubles the dosage of the maintenance dosage in order to reach high drug concentration at the initial stage.

Source: Internal clinical trial data

○ *In vitro studies against different HER2 High cancers*. In an *in vitro* cell viability study on a panel of 14 HER2 High cancer cell lines, our KN026 showed (i) comparable or stronger tumor growth inhibition effects than the trastuzumab plus pertuzumab combination in all the 14 HER2 High cell lines, including significant differences in two breast cancer cell lines and two lung cancer cell lines; and (ii) comparable or stronger tumor growth inhibition effects than either trastuzumab or pertuzumab in all the 14 cell lines. See "—Pre-clinical Studies—Cell Proliferation Assays in HER2-overexpressing Cancers." The following graph illustrates the tumor growth inhibition rates against the 14 cell lines in the *in vitro* study.



★ indicates statistically significant difference (P<0.05).

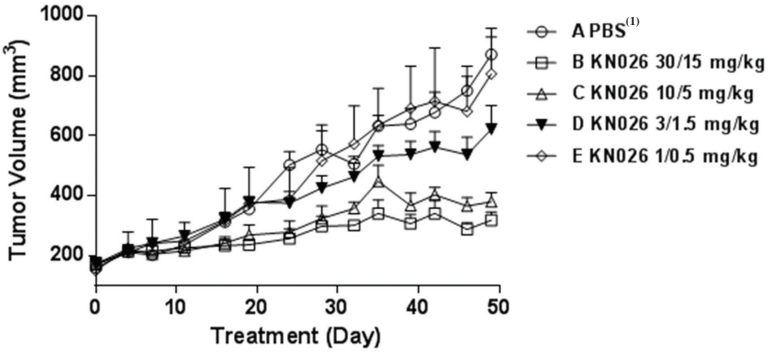
★★ Indicates strongly statistically significant difference (P<0.01).

(1) Trastuzumab was Herceptin purchased from Roche. Pertuzumab was a biosimilar to Perjeta produced by us in-house.

(2) SK-BR-3 cell line, BT474 cell line, AU565 cell line, ZR-75-30 cell line, MDA-MB-453 cell line, HCC2218 cell line and HCC1419 cell line are breast cancer cell lines; NCI-H2170 cell line, VMRC-LCP cell line and CALU-3 cell line are lung cancer cell lines; NCI-N87 cell line and NUGC-4 cell line are gastric cancer cell lines; KYSE-410 cell line and OE19 cell line are esophageal cancer cell lines.

Source: Wei H, Cai H, Jin Y, et al. Structural basis of a novel heterodimeric Fc for bispecific antibody production. Oncotarget 2017, 8(31): 51037. DOI: http://www.alphamabonc.com/uploads/2018/10/091612103465.pdf

- *Inhibition activities for HER2 Low lung cancer.* For HER2 cancers with low or intermediate expression levels, our KN026 demonstrated a dose-dependent tumor growth inhibition on a HER2 Low NSCLC NCI-H522 cell line. The study showed that KN026 at 30.0/15.0 mg/kg and 10.0/5.0 mg/kg significantly reduced tumor volume during the period from day 24 to day 49. See "—Pre-clinical Studies—Xenograft Tumor Model against HER2 Low Cell Line." The following graph illustrates the dose-dependent inhibitory effect on tumor growth on the NSCLC NCI-H522 cell line.



(1) The group receiving PBS was a negative control group.

Source: Internal clinical trial data

Pre-clinical Studies

Xenograft Tumor Model Against HER2 High Cell Line

The purpose of this study was to compare the tumor growth inhibition effect of our KN026 and the trastuzumab plus pertuzumab combination in a xenograft tumor model using a NSCLC Calu-3 cell line. To initiate the tumor xenografts, 24 mice were subcutaneously administered with HER2 High NSCLC Calu-3 cells. When the average volume of the xenograft tumors reached approximately 100 mm^3, these tumor-bearing mice were randomly divided into four groups with six mice in each group. One negative control group received PBS, the three other groups received intraperitoneal injections of our KN026 at 4.0/2.0 mg/kg, trastuzumab at 2.0/1.0 mg/kg in combination with pertuzumab at 2.0/1.0 mg/kg, or trastuzumab at 4.0/2.0 mg/kg in combination with pertuzumab at 4.0/2.0 mg/kg. The combination therapy with each agent at 2.0/1.0 mg/kg is equivalent to the dose level of KN026 at 4.0/2.0 mg/kg in terms of total molar mass. The combination therapy with each agent at 4.0/2.0 mg/kg is equivalent to two-fold the dose level of KN026 at 4.0/2.0 mg/kg in terms of total molar mass. Mice in the treatment group receiving KN026 and mice in the combination treatment (4.0/2.0 mg/kg plus 4.0/2.0 mg/kg) group had significantly reduced tumor volumes. KN026 at the 4.0/2.0 mg/kg dose level demonstrated a better tumor growth inhibition effect than the combination at 2.0/1.0 mg/kg plus 2.0/1.0 mg/kg. See "—Potential Advantages of KN026—Better potency than trastuzumab plus pertuzumab against HER2 High cancers—*In vivo* studies against HER2 High NSCLC."

Xenograft Tumor Model Against HER2 Low Cell Line

The purpose of this study was to determine the anti-tumor activities of our KN026 in a xenograft tumor model using a NSCLC NCI-H522 cell line that expresses low levels of HER2. The tumor model was developed by subcutaneous inoculation of NCI-H522 tumor cells into 30 male mice. When the average volume of the xenograft tumors reached approximately 170 mm^3, these tumor-bearing mice were randomly divided into five groups, with six mice in each group. Four groups received intraperitoneal injections of KN026 at 30.0/15.0 mg/kg, 10.0/5.0 mg/kg, 3.0/1.5 mg/kg and 1.0/0.5 mg/kg once per week for a total of eight times. One group was given PBS as a negative control group. The results showed that our KN026 had a dose-dependent inhibitory effect on the HER2 Low NSCLC NCI-H522 tumor growth. See "—Potential Advantages of KN026—Inhibition activities for HER2 Low lung cancer."

Cell Proliferation Assays in HER2-overexpressing Cancers

The purpose of this study was to assess the anti-tumor activities of our KN026 in various HER2 High cell lines for different cancers. 14 types of exponentially growing cells were plated into 96-well plates at 1×10^4 cells per well. KN026, trastuzumab, pertuzumab and the trastuzumab plus pertuzumab combination were then added after four hours at different concentrations. After six days of treatment, cell viabilities were determined using a cell viability assay, and the intensity was measured by a SpectraMax M5 plate reader. Raw values were calculated to evaluate the proliferation inhibition rates of the antibodies. Among the 14 cell lines, SK-BE-3 cell line, BT474 cell line, AU565 cell line, ZR-75-30 cell line, MDA-MB-453 cell line, HCC2218 cell line and HCC1419 cell line are breast cancer cell lines; NCI-H2170 cell line, VMRC-LCP cell line and CALU-3 cell line are lung cancer cell lines; NCI-N87 cell line and NUGC-4 cell line are GC cell lines; and KYSE-410 cell line and OE19 cell line are esophageal cancer cell lines. The results showed that our KN026 has (i) comparable or stronger tumour inhibition effects than the trastuzumab plus pertuzumab combination in all the 14 HER2 cell lines, including stronger inhibition effects on two breast cancer cell lines and two lung cancer cell lines with statistically significant difference; and (ii) comparable or stronger tumor growth inhibition effects than either trastuzumab or pertuzumab in all the 14 cell lines. See "—Potential Advantages of KN026—Better potency than trastuzumab plus pertuzumab against HER2 High cancers—*In vitro* studies against different HER2 High cancers."

Summary of Clinical Results

Phase I Clinical Trial in China (KN026-CHN-001)

We are conducting a first-in-human, open-label, phase I clinical trial of our KN026 as a single agent in China, consisting of a dose escalation phase Ia study and a dose expansion phase Ib study. The phase I study was initiated in September 2018 and is being conducted on adult subjects with (i) HER2 High; (ii) locally advanced or metastatic; and (iii) breast cancer or GC/GEJ, treatment naïve or progressed after at least one prior HER2-targeted therapy. As of September 20, 2019, 32 subjects were enrolled in the KN026-CHN-001 trial and had received at least one dose of KN026 per treatment. As of the Latest Practicable Date, the enrollment of the phase Ia study was completed and the enrollment of the phase Ib study was ongoing.

Study purpose. The purpose of the KN026-CHN-001 clinical trial is to evaluate the safety, tolerability and PK of KN026 monotherapy in adult subjects with HER2 High locally advanced or metastatic breast cancer and GC/GEJ in China. The primary objectives are to evaluate the safety, tolerability and determine the MTD and/or RP2D. The secondary objectives are to characterize the PK profile and to evaluate the preliminary efficacy of our KN026 as monotherapy.

Study design. The phase Ia dose escalation study has a classic "3+3" design. Subjects are receiving KN026 across four cohorts, including 5.0 mg/kg and 10.0 mg/kg QW, 20.0 mg/kg Q2W, and 30.0 mg/kg Q2W or Q3W. The phase Ib dose expansion study would be conducted based on the RP2Ds determined in the phase Ia study, which were 20 mg/kg Q2W and 30 mg/kg Q3W. Safety and tolerability will be assessed by monitoring TEAEs. Tumor assessments will be performed based on RECIST version 1.1.

Safety. As of September 20, 2019, all 32 subjects enrolled in the KN026-CHN-001 trial had breast cancer and were included in the safety data analysis. 23 subjects remained on the study treatment. Nine subjects had discontinued treatment, including eight due to disease progression and one due to treatment-related TEAE (one grade 3 ventricular arrhythmia). The median duration of exposure of KN026 was eight weeks, ranging from two weeks to 46 weeks. No subject had experienced DLTs.

As of September 20, 2019, 26 (81.3%) out of the 32 subjects had experienced treatment-related TEAEs. Three (9.4%) subjects had grade 3 or higher grade TEAEs. Three (9.4%) subjects had experienced treatment-related SAEs. One (3.1%) subject had experienced a TEAE leading to treatment discontinuation. Details of the TEAEs observed from all 32 subjects are summarized in the following table.

TEAE categories[1]	5.0 mg/kg QW (N=3)	10.0 mg/kg QW (N=3)	20.0 mg/kg Q2W (N=23)	30.0 mg/kg Q3W (N=3)	Total (N=32)
			n (%)		
All TEAEs	3 (100%)	2 (66.7%)	20 (87.0%)	2 (66.7%)	27 (84.4%)
TEAE, Grade ≥ 3	0	0	3 (13.0%)	0	3 (9.4%)
Treatment-related TEAEs	3 (100%)	2 (66.7%)	19 (82.6%)	2 (66.7%)	26 (81.3%)
Treatment-related TEAE, Grade ≥ 3	0	0	2 (8.7%)	0	2 (6.3%)
SAE	0	0	3 (13.0%)	0	3 (9.4%)
Treatment-related SAE[2]	0	0	3 (13.0%)	0	3 (9.4%)
TEAEs leading to permanent treatment discontinuation	0	0	1 (4.3%)	0	1 (3.1%)
Treatment-related TEAE leading to permanent treatment discontinuation	0	0	1 (4.3%)	0	1 (3.1%)
Treatment-related TEAE leading to death	0	0	0	0	0

(1) Reported under National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.

(2) Including one grade 2 interstitial pneumonitis, one grade 3 ventricular arrhythmia and one grade 3 transaminase increased occurred in three subjects from the 20.0 mg/kg Q2W cohort, respectively.

Source: Internal clinical trial data

The table below summarizes the most frequent treatment-related TEAEs in the KN026-CHN-001 trial as of September 20, 2019 (all grades ≥ 10%, or any ≥ grade 3).

Treatment-related TEAEs by Preferred Term[1]	5.0 mg/kg QW (N=3)		10.0 mg/kg QW (N=3)		20.0 mg/kg Q2W (N=23)		30.0 mg/kg Q3W (N=2)		Total (N=32)	
	All grades	Grade ≥ 3	All grades	Grade ≥ 3	All grades	Grade ≥ 3	All grades	Grade ≥ 3	All grades	Grade ≥ 3
					n (%)					
Fever	1 (33.3%)	0	1 (33.3%)	0	7 (30.4%)	0	1 (33.3%)	0	10 (31.3%)	0
Diarrhoea	1 (33.3%)	0	1 (33.3%)	0	2 (8.7%)	0	1 (33.3%)	0	5 (15.6%)	0
Aspartate aminotransferase increased	0	0	0	0	4 (17.4%)	0	1 (33.3%)	0	5 (15.6%)	0
Alanine aminotransferase increased	0	0	0	0	4 (17.4%)	0	0	0	4 (12.5%)	0
Hypokalemia	2 (66.7%)	0	1 (33.3%)	0	1 (4.3%)	0	0	0	4 (12.5%)	0
Blood creatinine increased	2 (66.7%)	0	1 (33.3%)	0	1 (4.3%)	0	0	0	4 (12.5%)	0
Ventricular arrhythmia	0	0	0	0	1 (4.3%)	1 (4.3%)	0	0	1 (3.1%)	1 (3.1%)
Transaminase increased	0	0	0	0	1 (4.3%)	1 (4.3%)	0	0	1 (3.1%)	1 (3.1%)

(1) Under Medical Dictionary for Regulatory Activities Preferred Terms.

Source: Internal clinical trial data

Efficacy. All 32 subjects enrolled in this KN026-CHN-001 trial are breast cancer patients that have received prior treatments including Herceptin. As of September 20, 2019, 21 subjects were evaluable subjects, and the preliminary efficacy analysis showed that one evaluable subject had a confirmed PR, five had unconfirmed PRs and nine had SD. 13 of the evaluable subjects remained on the study treatment. 11 subjects who had not reached the first post-baseline tumor assessment were excluded. The table below summarizes the best overall response in the efficacy analysis of the KN026-CHN-001 trial as of September 20, 2019.

Response	5.0 mg/kg QW (N=3)	10.0 mg/kg QW (N=3)	20.0 mg/kg Q2W (N=12)	30.0 mg/kg Q3W (N=3)	Total (N=21)	20.0 mg/kg Q2W and 30.0 mg/kg Q3W (N=15)
	n (%)					
Confirmed CR	0	0	0	0	0	0
Unconfirmed CR	0	0	0	0	0	0
Confirmed PR	0	0	1 (8.3%)	0	1 (4.8%)	1 (6.7%)
Unconfirmed PR	0	0	3 (25.0%)	2 (66.7%)	5 (23.8%)	5 (33.3%)
SD	2 (66.7%)	1 (33.3%)	5 (41.7%)	1 (33.3%)	9 (42.9%)	6 (40.0%)
PD	1 (33.3%)	2 (66.7%)	3 (25.0%)	0	6 (28.6%)	3 (20.0%)
$CR^{(1)}+PR^{(1)}$	0	0	4 (33.3%)	2 (66.7%)	6 (28.6%)	6 (40.0%)
DCR ($CR^{(1)}+PR^{(1)}+SD^{(2)}$)	2 (66.7%)	1 (33.3%)	9 (75.0%)	3 (100%)	15 (71.4%)	12 (80.0%)
Target Lesion Shrinkage	3 (100%)	2 (66.7%)	11 (91.7%)	3 (100%)	19 (90.5%)	14 (93.3%)

Abbreviations: CR=complete response, PR=partial response, SD=stable disease, PD=progressive disease, DCR=disease control rate.

(1) Including confirmed and unconfirmed responses.

(2) Lasting for at least six weeks.

Source: Internal clinical trial data

The following table further sets forth details of the best overall response at various scans and number of lines of prior treatment received of the 21 evaluable subjects as of September 20, 2019.

Patient No.	Classified response (as of September 20, 2019)	Change of target lesions from baseline (%)	Duration of treatments (days)	End of patient treatment (Yes/No)	Change of target lesions from baseline at respective tumor assessment cycle (%)										Cohort	Number of lines of prior HER2 targeted treatment[1]	Number of lines of prior treatment including chemo regimen
					1		2		3		4		5				
1	PR	(100%)	168	N	PR	(100%)	PR	(100%)	PR	(100%)	–	–	–	–	20.0 mg/kg Q2W	2	3
2	uPR	(61%)	105	N	SD	(24%)	PR	(61%)	–	–	–	–	–	–	30.0 mg/kg Q3W	2	2
3	uPR	(37%)	56	N	PR	(37%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	1	1
4	uPR	(35%)	105	N	SD	(21%)	PR	(35%)	–	–	–	–	–	–	30.0 mg/kg Q3W	2	5
5	uPR	(33%)	56	N	PR	(33%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	4	4
6	uPR	(32%)	84	N	PR	(32%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	2	4
7	SD	(26%)	105	N	SD	(19%)	SD	(26%)	–	–	–	–	–	–	30.0 mg/kg Q3W	2	4
8	SD	(25%)	84	N	SD	(25%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	2	3
9	SD	(24%)	56	N	SD	(24%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	1	1
10	SD	(23%)	170	Y	SD	(23%)	SD	(23%)	SD	(19%)	PD[2]	7%	–	–	20.0 mg/kg Q2W	6	6
11	PD	(23%)	84	Y	SD	(23%)	PD[2]	11%	–	–	–	–	–	–	5.0 mg/kg QW	11	14
12	SD	(21%)	69	N	SD	(21%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	2	2
13	SD	(14%)	130	Y	SD	(2%)	SD	(14%)	PD[2]	10%	–	–	–	–	5.0 mg/kg QW	3	4
14	PD[3]	(13%)	42	Y	SD	(13%)	–	–	–	–	–	–	–	–	10.0 mg/kg QW	2	2
15	PD	(12%)	84	N	SD	(12%)	PD	59%	–	–	–	–	–	–	20.0 mg/kg Q2W	3	3
16	SD	(7%)	126	Y	SD	(1%)	SD	(7%)	SD[4]	(1%)	–	–	–	–	10.0 mg/kg QW	2	3
17	PD	(5%)	42	Y	PD	(5%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	3	3
18	SD	(5%)	56	N	SD	(5%)	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	4	4
19	SD	(1%)	323	N	SD	(1%)	SD	12%	SD	13%	SD	12%	SD	10%	5.0 mg/kg QW	6	7
20	PD	22%	42	Y	PD	22%	–	–	–	–	–	–	–	–	20.0 mg/kg Q2W	3	6
21	PD	27%	42	Y	PD	27%	–	–	–	–	–	–	–	–	10.0 mg/kg QW	12	15

Abbreviations: PR=partial response, uPR=unconfirmed partial response, SD=stable disease, PD=progressive disease.

(1) HER2 targeted treatments include trastuzumab, lapatinib, HER2 ADC, and pyrotinib.

(2) Target lesion is considered as PD, taking the smallest sum on study as reference according to RECIST 1.1. However, % reduction in target lesion shown represents comparison with initial tumor baseline.

(3) This subject had PD despite reduction of target lesion, due to both non-target lesion unequivocal progression and development of new lesion.

(4) This subject developed new lesion on the third assessment cycle.

Source: Internal clinical trial data

All of the evaluable enrolled subjects had received multiple lines of prior treatments with HER2 targeted therapies. Key findings include:

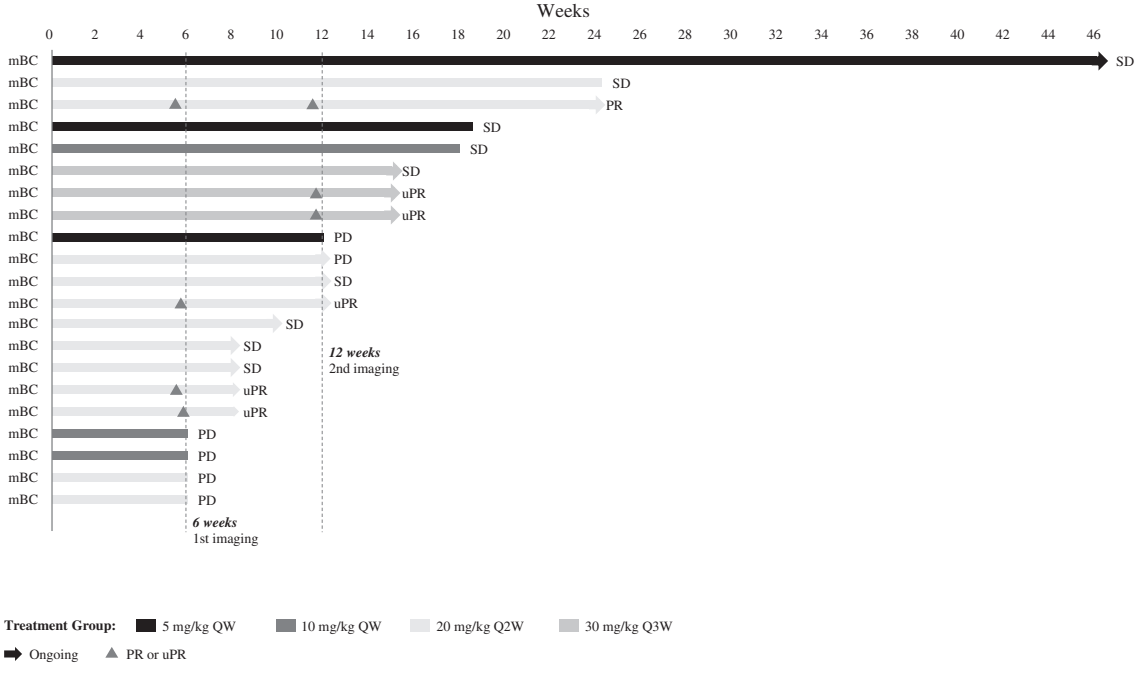
- The breast cancer patient with a confirmed PR failed a prior first-line treatment with Herceptin and a second-line treatment with lapatinib;

- Five subjects achieved unconfirmed PRs, with trends of improving tumor reduction effect in two subjects that were assessed through two scans; and

- Among the nine breast cancer patients with SD, we had one SD subject who had received one prior line of HER2-targeted treatment, four SD subjects who had received two prior lines of HER2-targeted treatments, and four SD subjects who had previously been heavily treated with three to six lines of HER2-targeted treatments.

Among the 21 evaluable subjects, 12 subjects had a treatment duration of at least 12 weeks, out of which eight subjects remained on the study treatment. The following swimming lane graph illustrates the treatment duration and the best overall responses of all the enrolled subjects in the phase I clinical trial in China as of September 20, 2019.

KN026-CHN-001

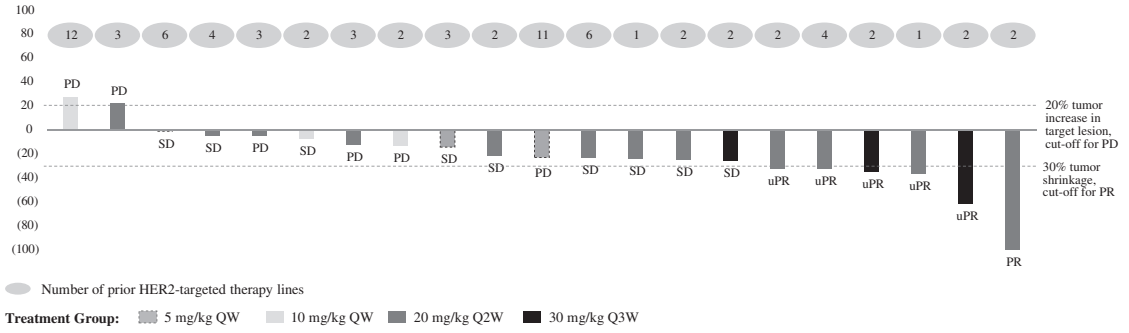


Abbreviations: PR=partial response, uPR=unconfirmed partial response, SD=stable disease, PD=progressive disease.

Source: Internal clinical trial data

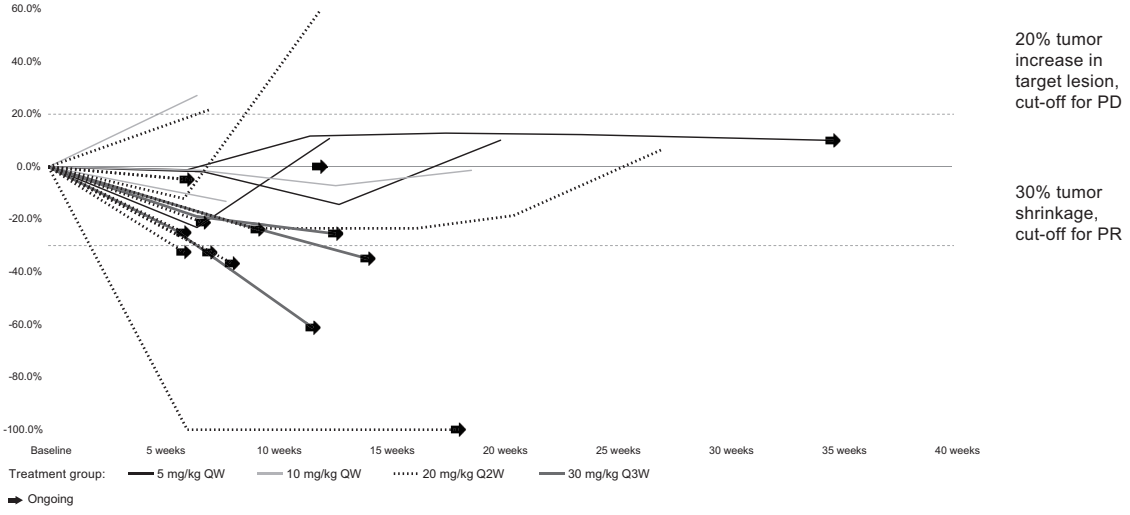
Among the 21 evaluable subjects, tumor reduction was observed in 14 out of 15 subjects receiving 20.0 mg/kg Q2W or 30.0 mg/kg Q3W (RP2Ds). The following waterfall plot shows the best overall response of the 21 breast cancer patients receiving KN026 as measured by percentage of change of target lesions from baseline based on CT/MRI scans.

Tumor Target Lesion Shrinkage from Baseline (%)



Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response.
Source: Internal clinical trial data

The following spider plot shows the change of target lesions across treatment duration of the 21 evaluable subjects receiving KN026 as of September 20, 2019. The spider plot demonstrated a trend of pronounced tumor control with longer treatment duration for some subjects.



Abbreviations: PR=partial response, SD=stable disease, PD=progressive disease, uPR=unconfirmed partial response.
Source: Internal clinical trial data

PK profile. The PK profile was evaluated after the first dose of KN026. As of September 20, 2019, a total of 11 subjects were included in the PK characterization. Mean KN026 C_{max} and AUC_{0-t} increased approximately linearly with increasing dose level. The volumes of distribution and clearance were similar across doses. Average half-life of KN026 was approximately four days to nine days.

Ctrough (trough concentration) is the lowest concentration reached by a drug before the next dose is administered, which should be measured before the next dose in order to avoid overdosing. Ctrough of KN026 at day 22 well exceeded steady-state trough serum concentrations at proposed clinical dose levels of trastuzumab. Average Ctrough of KN026 at day 22 was 57 to 104 ug/ml at 5.0 mg/kg and 10.0 mg/kg and higher than the steady state Ctrough level of trastuzumab of 47.4 to 66.1 ug/ml at proposed clinical dose.

Conclusion. In the preliminary results of the KN026-CHN-001 trial, KN026 exhibited a favorable safety profile in subjects with HER2 High locally advanced breast cancer and preliminary efficacy results demonstrated promising anti-tumor activities.

Clinical Trial Development Plan

We are executing a comprehensive clinical trial development plan in China and the United States targeting an array of HER2-overexpressing cancer indications for our KN026, including as a monotherapy and in combination with other therapies, with the purpose of supporting the registration of KN026 for multiple HER2-overexpressing indications in China and the United States. The table below sets forth the details of the clinical trial development plan for our KN026.

Trial No.	Indication	Planned trial stage	Type of therapy	Primary objectives/ endpoints	Secondary objectives/ endpoints	Planned size	(Expected) trial initiation date[1]	Expected trial completion date[2]	Expected BLA submission date	Status	Location and competent authority	Current standard of care
KN026-CHN-001(a)[3]	HER2 High locally advanced or metastatic breast cancer and GC/GEJ	Phase Ia	Mono	Evaluate the safety, tolerability and determine MTD and RP2D	Characterize the PK profile and evaluate the preliminary efficacy	~12-24	September 2018	4Q 2019	Not applicable	Ongoing	China/NMPA	Chemo and trastuzumab
KN026-CHN-001(b)[3]	HER2 High locally advanced breast cancer and GC/GEJ (progressed after at least one prior HER2-targeted therapy)	Phase Ib	Mono			~12-24	June 2019	2Q 2020	Not applicable	Ongoing	China/NMPA	Chemo and trastuzumab

Trial No.	Indication	Planned trial stage	Type of therapy	Primary objectives/ endpoints	Secondary objectives/ endpoints	Planned size	(Expected) trial initiation date[1]	Expected trial completion date[2]	Expected BLA submission date	Status	Location and competent authority	Current standard of care
KN026-US-001[4]	HER2-overexpressing solid tumors, including but not limited to locally advanced or metastatic breast cancer or GC/GEJ	Phase I	Mono	Evaluate the safety, tolerability and determine MTD and RP2D	Characterize the PK profile and evaluate the preliminary efficacy	~72-84	June 2019	3Q 2021	Not applicable	Ongoing	US/FDA	Trastuzumab, pertuzumab and chemo for breast cancer; trastuzumab and chemo for GC
KN026-CHN-202[5]	2L HER2-overexpressing GC/GEJ	Phase II	Mono	BOR and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters and ADAs	~ 40	June 2019	3Q 2021	Not applicable	Ongoing	China/NMPA	Not available
KN026-CHN-301[6]	1L HER2 High metastatic breast cancer	Phase III	Combo (with chemo)	PFS	Evaluate overall survival, BOR, TEAEs, PK parameters and ADAs	Not yet available	2Q 2020	4Q 2023	2Q 2024	Planning stage	China/NMPA	Chemo and trastuzumab
KN026-CHN-004[7]	≥2L HER2 High urothelial cancer ≥2L HER2 High ovarian cancer ≥2L HER2 High locally advanced unresectable or metastatic GC ≥2L HER2 High non-GC gastrointestinal cancer	Phase II	Combo (with KN046)	BOR and DOR according to RECIST 1.1	Evaluate TEAEs, PK parameters and ADAs	Not yet available	3Q 2020	2Q 2022	4Q 2022	Planning stage	China/NMPA	Not available

Abbreviations: 1L=first-line, 2L=second-line, mono=monotherapy, combo=combination therapy, chemo=chemotherapy, GC=gastric cancer, GEJ=gastroesophageal junction cancer.

(1) Denotes the date on which the first patient was enrolled.

(2) Denotes the date on which the last visit was made by the patient.

(3) Two parts of KN026-CHN-001 trial, a multi-center, open-label, single arm clinical trial.

(4) A multi-center, open-label, single arm clinical trial. Depending on clinical data from the KN026-CHN-001 trial and KN026-US-001 trial, we are exploring the possibility of initiating a pivotal trial for the third line or late line treatments of breast cancer. As of the Latest Practicable Date, we enrolled six subjects in this trial.

(5) A multi-center, open-label, single arm clinical trial. As of the Latest Practicable Date, we enrolled seven subjects in this trial.

(6) A multi-center, randomized, active controlled clinical trial.

(7) A multi-center, open-label, single arm clinical trial. If promising efficacy signals are observed in a majority of the selected indications, we plan to expand the basket trial into a pivotal trial.

As HER2 High cancers are expected to be the most responsive to anti-HER2 antibody drugs, we plan to strategically focus on HER2 High cancers in our KN026 clinical development plan. In addition, considering the efficacy in HER2 Low cancers exhibited by our KN026 in pre-clinical studies, we also plan to explore the efficacy of KN026 in cancers with low to intermediate expression levels. We have selected breast cancer and GC/GEJ, two proven and major indications sensitive to anti-HER2 antibody drugs for near-term development:

- *Metastatic breast cancer (mBC)*. In China, approximately 40% of breast cancers are metastatic and the combination therapy of trastuzumab, pertuzumab and chemotherapy, the first-line standard of care in the United States, is not approved China.

- *Gastric/gastroesophageal junction cancers (GC/GEJ)*. GC/GEJ are among the most common cancers in China. The five-year survival rates for such cancers range from 25% to 35%.

With the expectation to further improve response rates and maximize the market value of our pipeline products, we plan to apply the combination therapy of our KN026 and KN046 on HER2 High gastric cancer and other gastrointestinal cancers, urothelial cancer and ovarian cancer, a group of cancers that are prevalent in China. In addition, studies have suggested that the trastuzumab and pertuzumab combination therapy reached an ORR of 33.3% in urothelial cancer patients. Therefore, we believe that the KN026/KN046 combination can potentially offer a superior ORR and DOR, which may translate into a further improved overall survival benefit and enable a chemotherapy-free first-line therapy for urothelial cancer. If promising efficacy signals are observed in a majority of the selected indications, we plan to expand the basket trial into a pivotal trial.

Competition

To date, there are no approved anti-HER2 BsAbs on the global market. As of August 31, 2019, there were three and seven anti-HER2 BsAb candidates in clinical trials in China and the United States, respectively. A total of three out of these BsAb drug candidates have a dual HER2/HER2 blockade, including our KN026, Mabwork's MBS301 and Zymeworks's ZW25.

To date, the two most widely prescribed anti-HER2 mAbs on the market are trastuzumab and pertuzumab. The combination therapy of trastuzumab, pertuzumab and chemotherapy is the only approved HER2/HER2 dual blockade therapy and has demonstrated improved treatment efficacy over trastuzumab in combination with chemotherapy. The combination therapy of trastuzumab, pertuzumab and chemotherapy is approved for HER2 High metastatic breast cancer and as neoadjuvant/adjuvant treatments for HER2 High early breast cancer in the United States. In China, this combination therapy is approved only as the adjuvant or neoadjuvant treatment for HER2 High early breast cancer and is currently in phase III clinical trials for the treatment for HER2 High metastatic breast cancer. For approved anti-HER2 monospecific antibodies, see "—Current Anti-HER2 Antibody Drugs and Limitations." There are also a number of anti-HER2 monospecific antibody candidates in clinical trials or later stage, including certain biosimilar candidates of trastuzumab and pertuzumab in China and the United States.

Details of anti-HER2 BsAb drug candidates and major late-stage monospecific antibody candidates as of August 31, 2019 that may compete with our KN026 in China and the United States are set out in the following table.

Anti-HER2 BsAb Candidates

Drug candidate names	Company	Target(s)	Indications	Clinical stage	First posted date
PRC					
KN026	Alphamab	HER2/HER2	HER2-overexpressing GC/GEJ	Phase II	May-2019
			HER2 High breast cancer, GC/GEJ	Phase I	Aug-2018
MBS301	Beijing Mabworks Biotech Co., Ltd.	HER2/HER2	HER2 High breast cancer, GC	Phase I	Mar-2019
M802	Wuhan YZY Biopharma Co., Ltd.	HER2/CD3	HER2 High solid tumors	Phase I	Jul-2018
U.S.					
ZW25	Zymeworks	HER2/HER2	HER2 High GEJ	Phase II	Apr-2019
			HER2 High cancer	Phase I	Sep-2016
KN026	Alphamab	HER2/HER2	HER2 High breast cancer, GC/GEJ	Phase I	Feb-2019
MCLA-128	Merus	HER2/HR3	Breast cancer	Phase II (with trastuzumab)	Oct-2017
HER2 BATs	Merck	HER2/CD3	Breast cancer	Phase I/II (with pembrolizumab)	Sep-2016
PRS-343	Pieris Pharmaceuticals	HER2/CD137	HER2 High breast cancer, GC, bladder cancer, solid tumors	Phase I (with atezolizumab)	Aug-2018
			HER2 High breast cancer, GC, bladder cancer, solid tumors	Phase I	Nov-2017
GBR 1302	Glenmark Pharmaceuticals, Ltd	HER2/CD3	Breast cancer	Phase I/II	Jun-2019
			HER2 High solid tumors	Phase I	Jul-2016
BTRC4017A	Roche	HER2/CD3	Solid tumors	Phase I	Feb-2018

Anti-HER2 Monospecific Antibody Candidates[3] (Phase III or Later stage)

Drug candidate names	Company	Target(s)	Indications	Clinical stage	First posted date
PRC					
Perjeta (pertuzumab)/ Trastuzumab[1]	Roche	HER2/HER2	HER2 High GC	Phase III	Apr-2014
			HER2 High GC/GEJ	Phase III	Apr-2014
			HER2 High breast cancer	Phase III	Mar-2015
Herceptin (trastuzumab)/ Pertuzumab[2]		HER2/HER2	HER2 High breast cancer	Phase III	Feb-2016
Perjeta (pertuzumab)		HER2	HER2 High breast cancer	Phase III	Jan-2015
U.S.					
Perjeta (pertuzumab)/ Trastuzumab[1]	Roche	HER2/HER2	HER2 High breast cancer	Phase III	Dec-2007
			HER2 High GC/GEJ	Phase III	Jan-2013
MGAH22 (Margetuximab)	MacroGenics, Inc.	HER2	HER2 High breast cancer	Phase III	Jul-2015

Abbreviations: GC = gastric cancer, GEJ = gastroesophageal junction cancer.
(1) Including trials of Perjeta in combination with any drugs with the generic name of trastuzumab.
(2) Including trials of Herceptin in combination with any drugs with the generic name of pertuzumab.
(3) This table does not include biosimilar candidates of trastuzumab or pertuzumab.
Source: FDA; NMPA; CIC Report (As of August 31, 2019)

Compared with the combination of trastuzumab and pertuzumab, our KN026 has demonstrated a better potency against HER2 High cancers in pre-clinical studies. See "—Potential Advantages of KN026—Better potency than trastuzumab plus pertuzumab against HER2 High cancers." In addition, our KN026 has shown efficacy in other HER2-overexpressing cancers in addition to breast cancer and GC/GEJ.

Material Communications and Next Steps

We received an Umbrella IND approval for KN026 from the NMPA and an IND approval from the FDA in March 2018 and October 2018, respectively. We plan to conduct a number of clinical trials for different cancer indications in 2019 and 2020. To date, none of these authorities have raised any objections or material concerns with respect to the development of KN026.

CTLA-4 Fusion Protein Candidate – KN019

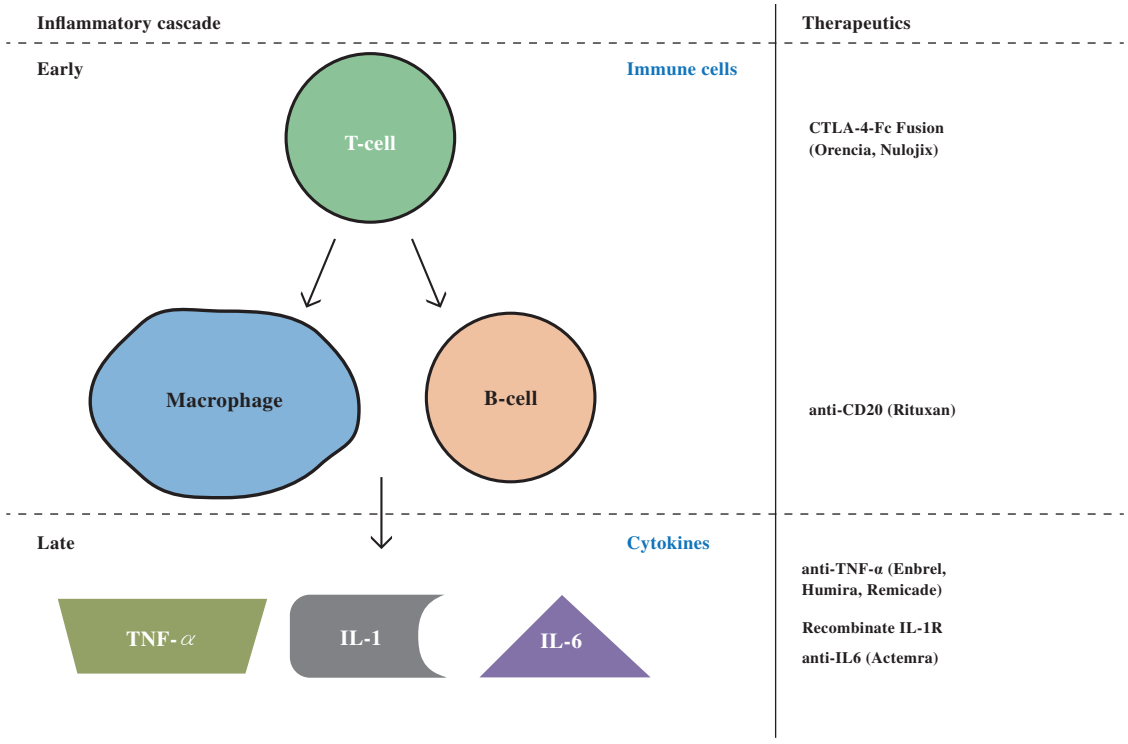
Overview

We are developing KN019, a CTLA-4-based immunosuppressant fusion protein drug candidate. KN019 functions at the early stage of T-cell activation and therefore may lead to efficient global downregulation of unwanted immune responses. Globally, the only two approved CTLA-4-Fc fusion proteins are Nulojix (belatacept) and Orencia (abatacept). Orencia is approved for RA, idiopathic arthritis and psoriatic arthritis with global sales of US$2.7 billion in 2018. Nulojix is an improved version of Orencia with higher potency and is approved for post-transplant kidney rejection. Our KN019 has the same amino acid sequence as belatacept. Belatacept has not been approved for marketing in China and we plan to develop

KN019 under the new drug pathway according to the NMPA regulations. Considering the immunosuppressant properties of KN019, it has potential broad applications in both autoimmune diseases and oncology treatment-induced immune disorders. We plan to start phase II trial of RA in August of 2019 and expand to oncology treatment-induced immune disorder indications in the future.

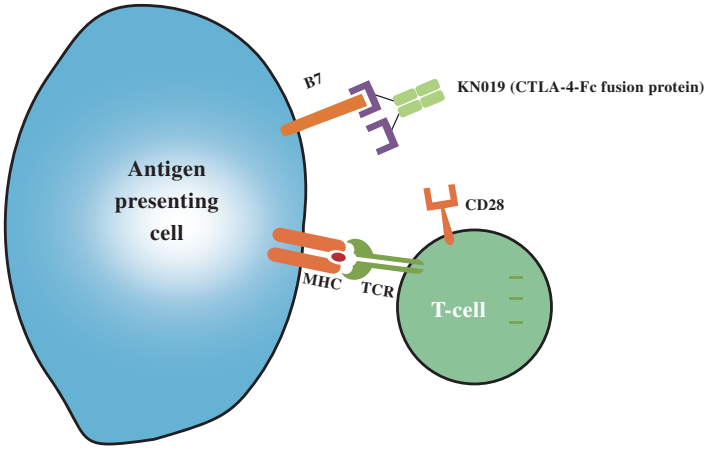
Mechanism of Action

Immunosuppressant drugs are a class of drugs that suppress or reduce the strength of the body's immune system to prevent it from attacking normal cells. Immunosuppression can be achieved by depleting immune cells, diverting immune cell traffic, or blocking immune response pathways. T-cells, a major type of immune cells, affect the upstream immune response process. The following diagram illustrates the different major lymphocytes and signals for activation and maintenance of immune responses.



Source: CIC Report

Our KN019 is a CTLA-4-Fc fusion protein, a biological immunosuppressant agent that blocks the T-cell response pathway. The stimulation of immunological response requires participation of signaling through the binding of B7 on APCs to CD28 on T-cells. CTLA-4 can compete with CD28 in binding to B7. Binding of B7 receptors to CTLA-4 results in an inhibitory signal to T-cells. KN019 blocks the specific interaction of B7 receptors to CD28, thereby prevents over-activation of the immune system. The following diagram illustrates the mechanism of action of our KN019 as an immunosuppressant.



* CTLA-4 can compete with CD28 in binding to B7. Binding of B7 receptors to CTLA-4 inhibits T-cell activation. KN019, as a CTLA-4-Fc fusion protein, binds to B7 to prevent over-activation of the immune system.

Positioning of KN019

With a focus on oncology biologics, we intend to develop KN019 into a supportive therapy to oncology treatments, especially immuno-oncology treatments. Oncology treatments may induce immune disorders, such as severe irAEs, GvHD and CRS, which can become life-threatening if not managed appropriately. KN019, as a CTLA-4-Fc fusion protein abrogating T-cell co-stimulation, could be an option for managing these conditions. Compared with certain immunosuppressant drugs that function at later stages of immune responses, KN019 functions at the early stage of T-cell activation and therefore may lead to efficient global downregulation of unwanted immune responses. KN019 specifically reverses the CTLA-4 pathway activated by immune checkpoint inhibition, and therefore we believe it has potential to reduce off-target side effects and achieve effective immunosuppression.

BMS's Orencia (abatacept) and Nulojix (belatacept) are the only two approved CTLA-4-Fc fusion proteins acting as T-cell immunosuppressant drugs worldwide. Currently, Nulojix (belatacept) is approved for prophylaxis of organ rejection in adults receiving a kidney transplant and Orencia (abatacept) is approved for RA, idiopathic arthritis and psoriatic arthritis. Our KN019 has the same amino acid sequence as Nulojix, an improved version of Orencia with higher potency. Therefore, considering the immunosuppressant properties of KN019, we plan to formulate a two-prong clinical strategy focusing on (i) RA indications such as RA and prophylaxis of post-transplant kidney rejection in the near term, and (ii) oncology treatment-induced immune disorders in the longer term. More specifically, we intend to develop KN019 drug into an oncology supportive therapy to treat oncology treatment-induced immune disorders, such as severe irAEs, GvHD and CRS.

Current Therapies of KN019's Indications in China

TNF-α Inhibitor Refractory RA

On the global market, different types of biologics can be used in RA patients previously treated with TNF-α inhibitors, including Orencia (abatacept, a CTLA-4-Fc fusion protein), Actemra (IL-6 inhibitor), Rituxan (CD20 inhibitor) and Kineret (IL-1 inhibitor). They have different mechanisms of action and no head-to-head comparisons have been made. In China, currently only Actemra is approved for TNF-α refractory RA treatment.

Indication for Post-transplant Kidney Rejection

In China, the current primary treatment for suppression of post-transplant kidney rejection are CNI drugs, such as cyclosporine regimens. However, CNI-based regimens may not adequately preserve the allograft function for an extended period due to side effects caused by long-term use.

Advantages of KN019

KN019 functions at the early stage of T-cell activation and enables efficient global downregulation of T-cell-mediated immune responses. Unlike broad-spectrum immunosuppressants which affect many types of immune cells and are associated with numerous adverse events, KN019 specifically inhibits the CD28-B7 pathway activated by immune checkpoint inhibitors, thus reversing adverse immune disorders triggered by immune checkpoint inhibitors, with limited off-target effects.

TNF-α Inhibitor Refractory RA

KN019 is an improved version of Orencia, a CTLA-4 fusion protein developed by BMS for the treatment of TNF-α inhibitor refractory RA. Compared with IL-6 inhibitors, we believe KN019 potentially has better efficacy because, unlike IL-6 inhibitors which only inhibit downstream signaling of IL-6, KN019 inhibits T-cell activation at early stages in the pathogenic cascade of RA.

Indication for Prophylaxis of Post-transplant Kidney Rejection

Belatacept has been approved for the treatment of post-transplant kidney rejection in the United States. A BMS study has shown that patients treated with belatacept have significantly higher long-term patient and graft survival than those treated with cyclosporine. In light of the high similarity of KN019 to belatacept, we believe KN019 can achieve comparable safety and efficacy.

CMC and Analytical Characterization

Our KN019 has an identical amino acid sequence to Nulojix (belatacept) of BMS. KN019 is a CTLA-4-Fc fusion protein candidate with complicated glycolysation. Certain important properties of belatacept, including pharmacokinetics, immunogenicity and stability are closely associated with the post-translational structure of proteins. Therefore, we have performed extensive analyses to confirm the comparability of KN019 and Nulojix with respect to their physicochemical and biological properties, including the following analyses.

Amino Acid Structure

The amino acid sequences and disulphide bonds are the core structure of a protein, and it is a fundamental aspect in demonstrating biosimilarity. We have conducted peptide mapping to compare the amino acid sequence and disulphide bonds of KN019 and belatacept (three lots of each). The highly similar spectra patterns indicate that KN019 has the same amino acid sequence and disulphide bond as belatacept.

Post Translational Modification

Protein glycosylation is a post-translational modification process that directly affects protein function. The presence of glycans can modify the structure (protein folding or accessibility to enzymes) or function directly. KN019 has glycosylation sites in both the CTLA-4 domain and the Fc region, and the glycosylation sites are occupied with complex mixture of different glycans. We released a mixture of glycans from each of KN019 and belatacept (three lots for each) enzymatically. The three lots of KN019 demonstrated similar patterns to the three lots of belatacept, in terms of types and content of glycans.

Pre-clinical Studies

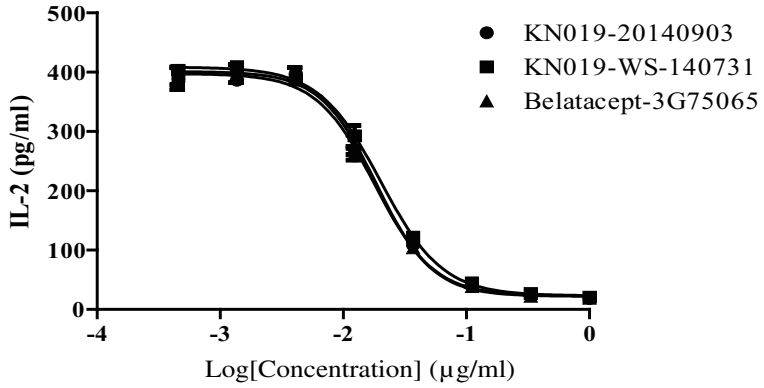
We have performed comprehensive pre-clinical studies on KN019 and the results indicated that KN019 is highly similar to Nulojix in bioactivity and PK.

Inhibition of Secretion of IL-2

Study purpose. The purpose of this study was to compare the inhibition effect on the T-cell activation by KN019 and belatacept in the Jurkat T-cell/Raji cell mixed lymphocytes reactions.

Study design. CTLA-4 binding to B7 inhibits proliferation and accumulation of the primary T-cell growth factor, IL-2. Jurkat T-cells were pre-incubated in the presence of anti-human CD3 in a plate. Two lots of KN019 and one lot of belatacept with various concentrations with a fixed concentration of Raji cell were added to Jurkat T-cells. After 24 hours, the secretion level of IL-2 was assessed. The inhibition activity of IL-2 was assessed in terms of EC_{50}.

Results. Both KN019 and belatacept had dose-dependent inhibition of secretion of IL-2. The inhibitory effect of KN019 was comparable to that of belatacept. The following graph shows the levels of IL-2 after administration of KN019 and belatacept.



(1) KN019-20140903 and KN019-WS-140731 are two lots of KN019 produced by us in-house. Belatacept is Nulojix purchased from BMS.

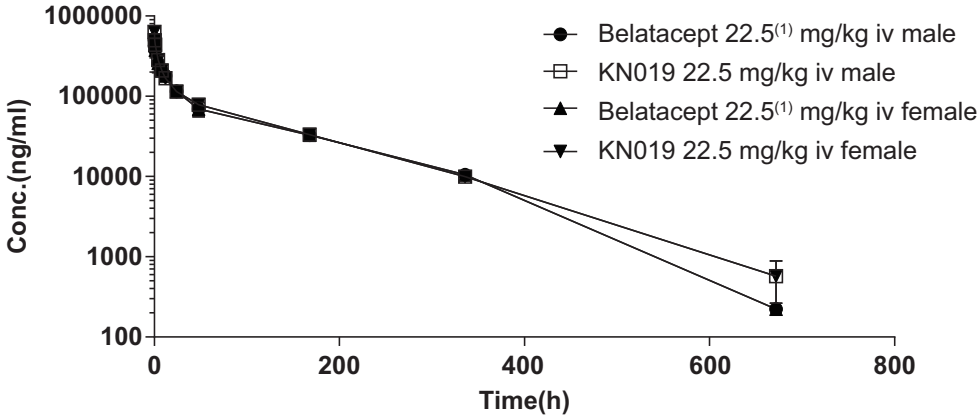
Source: IND Application File to NMPA

PK Profile

Study purpose. The purpose of this study was to determine the similarity in the PK profiles between KN019 and belatacept.

Study design. Four groups of cynomolgus monkeys were included in this study, each group had three females and three males. One group received a single dose of KN019 at 22.5 mg/kg, and another group received a single dose of belatacept at the same dosage. Blood sampling was performed at different time points up to 45 days after the dosage.

Results. The PK profiles in the pre-clinical study on cynomolgus monkeys of KN019 and belatacept were highly similar at the same dose level with no differences by gender. As illustrated in the graph below, after receiving a single dose at 22.5 mg/kg, there were no apparent differences in drug concentration between KN019 and belatacept at the same timing points throughout the study in female and male cynomolgus monkeys.



(1) Belatacept was Nulojix purchased from BMS.

Source: IND Application File to NMPA

Summary of Clinical Results

Phase I Clinical Trial Results (KN019-001)

We completed a phase I clinical trial of our KN019 as a single agent in healthy Chinese subjects in China (KN019-001) in January 2019.

Study purpose. The purpose of the phase I clinical trial was to evaluate the safety, tolerability and PK profile of KN019 in healthy subjects.

Study design. The phase I clinical trial was a double-blinded, placebo-controlled dose-escalation study. Subjects were randomly assigned into a KN019 group and a placebo control group at a ratio of approximately 4:1. The KN019 group received a single intravenous infusion of KN019 across five cohorts, including 0.5 mg/kg, 2.0 mg/kg, 5.0 mg/kg, 10.0 mg/kg and 20.0 mg/kg. The placebo control group received no drug. Safety was assessed by monitoring TEAEs.

Safety. The results showed that KN019 was generally safe and well tolerated in healthy subjects after a single intravenous infusion, and no relationship between the number of AEs and dose escalation was observed. 34 subjects were enrolled in the KN019-001 trial, with 27 subjects receiving KN019 across five cohorts and seven subjects assigned into the placebo control group. No infusion-related reactions or severe infection events were observed. Nine subjects experienced 17 drug-related AEs, all of which were grade 1. The most frequent drug-related AEs, were cough, white blood cells urine positive, and headache. No serious AEs were reported. There were no AEs causing subjects to withdraw from the study. Details of the AEs observed from all the 27 subjects receiving KN019 in the phase I clinical trial are summarized in the following table.

	KN019 Group						Placebo
AE categories[1]	**0.5 mg/kg (N=2)**	**2.0 mg/kg (N=3)**	**5.0 mg/kg (N=8)**	**10.0 mg/kg (N=8)**	**20.0 mg/kg (N=6)**	**Total (N=27)**	**group (N=7)**
				n (%)			
All AEs	0	2 (66.7%)	1 (12.5%)	3 (37.5%)	3 (37.5%)	9 (33.3%)	1 (14.3%)
AE, Grade ≥ 3	0	0	0	0	0	0	0
Drug-related AEs[2]	0	2 (66.7%)	1 (12.5%)	3 (37.5%)	3 (37.5%)	9 (33.3%)	1 (14.3%)
Drug-related AE, Grade ≥ 3	0	0	0	0	0	0	0
SAE	0	0	0	0	0	0	0
Drug-related SAE	0	0	0	0	0	0	0
Drug-related AE leading to death	0	0	0	0	0	0	0

(1) Reported under National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.

(2) The most frequent drug-related AEs (≥10%) were respiratory, thoracic, and mediastinal disorders (n=3, 11.1%), including cough, phlegmy cough and nasal congestion.

Source: Internal clinical trial data

PK/PD analysis. This trial analyzed receptor occupancy to see how KN019 binds to B7 and at which dose level this binding is optimal. The results showed B7 binding was inhibited by 50% with approximately 0.7 μg/ml of KN019. Additionally, maximum occupancy of B7 was achieved at approximately 70 μg/ml of KN019. The PK/PD analysis supports a Q4W dosing schedule.

PK profile. Linear PK was observed across dose levels between 2.0 mg/kg to 20.0 mg/kg, indicating that the PK profile of KN019 is dose-proportional. There were no characteristics or evidence of target-mediated drug disposition at lower serum antibody concentrations.

Conclusion. Our KN019 exhibited favorable safety and PK profiles and indicated good pharmacological effects in the phase I clinical trial in healthy subjects.

Clinical Trial Development Plan

The table below sets forth the details of our clinical trial development plan for our target indications of our KN019 for RA and post-transplant kidney rejection in China.

Trial No.	Indication	Planned trial stage	Type of therapy	Primary objectives/ endpoints	Secondary objectives/ endpoints	Planned size	(Expected) trial initiation date[1]	(Expected) trial completion date[2]	Expected BLA submission date	Status	Standard of care
KN019-001[3]	Not applicable	Phase I	Mono, intravenous formulation	Safety and tolerability	Evaluate PK and immunogenicity	27	December 2017	January 2019	Not applicable	Completed	Not applicable
KN019-201[4]	RA (targeting non-responders to TNF-α inhibitors)	Phase II	Mono, intravenous formulation	American college of rheumatology (ACR) criteria (standard criteria to evaluate the effectiveness of arthritis medications) at 24 weeks	Evaluate ACR criteria, HAQ-DI, DAS28-CRP, PK, immunogenicity, safety and tolerability	141	4Q 2019	August 2021	Not applicable	Preparation for initiation	Glucocorticoid, TNF-α inhibitors
KN019-002[5]	Not applicable	Bioavailability study	Mono, intravenous and subcutaneous formulation	PK	Evaluate safety and tolerability, and immunogenicity	32	1Q 2020	3Q 2020	Not applicable	Planning stage	Not applicable

Abbreviations: mono = monotherapy, HAQ-DI = Health Assessment Questionnaire – Disability Index, DAS28-CRP = Disease Activity Score 28-joint count C reactive protein.

(1) Denotes the date on which the first patient was enrolled.

(2) Denotes the date on which the last visit was made by the patient.

(3) A double-blinded, placebo-controlled dose-escalation trial in healthy subjects.

(4) A multi-center, open-label, single arm clinical trial.

(5) A bioavailability study in healthy subjects to switch the administration of KN019 from intravenous formulation to subcutaneous formulation.

We plan to register our KN019 for RA and post-transplant kidney rejection. For the RA indication, from the marketing perspective, our KN019 would primarily focus on patients with TNF-α refractory. See "—Positioning of KN019."

We have completed the KN019-001 trial in China. KN019 exhibited favorable safety and PK profile in this trial. See "—Summary of Clinical Results—Phase I Clinical Trial Results (KN019-001)." We plan to initiate a phase II clinical trial (KN019-201) in patients with RA through intravenous infusion commencing in the fourth quarter of 2019. As RA is a chronic autoimmune disease, the subcutaneous formulation is more convenient than intravenous administration for RA patients during a long-term treatment regimen, and can improve patient compliance and pharmacoeconomics benefits. In parallel with this phase II trial, we plan to conduct a bioavailability study (KN019-002) in healthy subjects in the first quarter of 2020 to switch the intravenous formulation to subcutaneous formulation for KN019 in preparation for the following trials for RA treatment and post-transplant kidney rejection, which are still in the planning stages.

Competition

There is no approved CTLA-4-Fc fusion protein for autoimmune diseases in China. Currently, KN019 and abatacept are the only two CTLA-4-Fc fusion protein candidates in the registration process in China. The following table sets forth the details of these two drug candidates.

Name	Developer	Development stage	Start of current stage	Indications	Route of entry
KN019	Alphamab	Phase I (completed)	January 2018	RA[(1)], post-transplant kidney rejection	Intravenous/ subcutaneous[(2)]
Abatacept	Jiangsu Simcere Pharmaceutical Co., Ltd./BMS	BLA	July 2018	RA	Subcutaneous

(1) Primarily focus on RA patients inadequately addressed by TNF-α inhibitors.

(2) Subcutaneous formulation will be applied in phase III clinical trials of KN019.

Source: NMPA; CIC Report (as of August 31, 2019)

For the RA indication, we expect our KN019 to have the same advantages of belatacept over abatacept. BMS conducted a pilot study to evaluate the safety, preliminary clinical activity and immunogenicity of multiple doses of abatacept and belatacept in subjects with RA. The study results showed that belatacept had a superior efficacy and safety profile for the RA indication compared to abatacept, especially in relatively lower dosages. KN019, with potentially comparable efficacy and safety profiles to belatacept, may have similar advantages over abatacept.

Indication for RA

In addition to abatacept, there are a number of approved drugs or drug candidates under development with indications covering TNF-α refractory RA. These drugs and drug candidates are differentiated by their targets, with each target representing a specific mechanism of action and potential advantages in addressing a specific cohort of RA patients. There have been no head-to-head comparisons made for these drugs. The following table sets forth information on these approved drugs and drug candidates as of August 31, 2019.

Approved Biologics for TNF-α Inhibitor Refractory RA in the PRC

Trade name (Generic name)	Company	Target	Route of entry	Date of approval
Actemra (tocilizumab)	Roche	IL-6	Intravenous	Mar-2013

Biologics Candidates for TNF-α Inhibitor Refractory RA in the PRC (Phase III or Later Stage)

Drug candidate name	Company	Target	Development stage	Route of entry	First posted date
Abatacept	Jiangsu Simcere Pharmaceutical Co., Ltd./BMS	B7	BLA	Subcutaneous	Jul-2018
RC18	RemeGen, Ltd.	BLyS/APRIL	Phase III	Subcutaneous	Nov-2016
Tocilizumab	Roche	IL-6	Phase III	Subcutaneous	Mar-2017
SM03	LonnRyonn Pharma Ltd.	CD22	Phase III	Intravenous	Dec-2017
HLX01	Shanghai Henlius Biotech, Inc.	CD20	Phase III	Intravenous	Aug-2018
BAT1806	Bio-Thera Solutions, Ltd	IL-6	Phase III	Intravenous	Feb-2019
CMAB806	Jinyu Bio-technology Co., Ltd.	IL-6	Phase III	Intravenous	Apr-2019
rhIL-1Ra	Changchun Institute of Biological Products Co., Ltd.	IL-1	Phase III	Intravenous	Apr-2019
LZM008	Livzon Biologics, Ltd.	IL-6	Phase III	Intravenous	May-2019

Source: NMPA; CIC Report (as of August 31, 2019)

Indication for Post-transplant Kidney Rejection

In addition to RA, we intend to pursue an indication for KN019 for post-transplant kidney rejection. There is no other T-cell suppressant CTLA-4 fusion protein approved or in the registration process for this indication in China except for KN019. Compared with CNI drugs, the current primary treatment, we expect our KN019 can potentially have better safety and efficacy results. See "—Advantages of KN019."

Material Communications and Next Steps

We received two IND approvals from the NMPA for KN019 for post-transplant kidney rejection and RA in June 2017 and September 2017, respectively. We are executing a comprehensive clinical trial development plan. To date, the NMPA has not raised any objections or material concerns with respect to KN019.

Anti-PD-L1 sdAb Candidate – KN035

Overview

We invented KN035 and currently are jointly developing it with 3DMed. KN035 is potentially the first subcutaneously injectable PD-L1 inhibitor worldwide. KN035 is being evaluated as a monotherapy and potentially in combination with other therapies in a number of clinical trials in China and overseas for an array of indications, including a phase II pivotal clinical trial for dMMR/MSI-H solid tumors and a phase III pivotal trial for BTC in China. The first BLA for KN035 is expected to be filed by the end of 2020 for dMMR/MSI-H solid tumors.

Under our partnership with 3DMed, 3DMed is responsible for clinical trials of KN035. We own the rights to manufacture and supply KN035 to 3DMed and are entitled to share the profits generated from KN035's global sales after its commercialization. See "—Our Collaboration Arrangements—Co-development Agreements with 3DMed."

Mechanism of Action

KN035 binds to PD-L1 and blocks it from binding to PD-1. For details of the PD-1/PD-L1 pathway and the blockade function, see "—Anti-PD-L1/CTLA-4 BsAb Candidate – KN046—Mechanism of Action."

KN035 is a monospecific antibody consisting of a sdAb and an Fc region. Due to the sdAb format, KN035 has half the molecular weight as compared to a full antibody, which enables it to have enhanced penetrability while possessing a full antigen-binding capacity. As such, we believe KN035 is an ideal building block for designing and producing multi-functional antibodies such as BsAbs. See "—Research and Development—Proprietary Platforms and Expertise—Single Domain Antibodies Used as an Alternative Scaffold." In addition, the Fc-mediated effector functions are muted in KN035 to limit its exposure to the immune system and avoid unwanted adverse immune responses.

Current Drugs and Limitations

As of the Latest Practicable Date, there were a total of six immune checkpoint inhibitors against PD-(L)1 in the global market, of which three target PD-1 and three target PD-L1. All six are monospecific antibodies. The three PD-1 inhibitors are BMS's Opdivo (nivolumab), Merck's Keytruda (pembrolizumab), and Sanofi S.A. and Regeneron Pharmaceuticals, Inc.'s Libtayo (cemiplimab). The three PD-L1 inhibitors are Roche's Tecentriq (atezolizumab),

Merck KGaA and Pfizer's Bavencio (avelumab) and AstraZeneca and MedImmune's Imfinzi (durvalumab). As of the same date, in China, there were five approved PD-(L)1 inhibitors, namely, BMS's Opdivo, Merck's Keytruda, Junshi's toripalimab, Innovent's Tyvyt (sintilimab) and Hengrui's camrelizumab. See "—Anti-PD-L1/CTLA-4 BsAb Candidate – KN046—Current Drugs and Limitations" and "Industry Overview—Overview of the Immune Checkpoint Inhibitor Market in the PRC and United States—Overview of PD-(L)1 Inhibitor Market in the PRC and United States—Competitive Landscape" for details.

All of these PD-(L)1 inhibitors are required to be administered intravenously. However, intravenous formulation is inconvenient for patients because it requires frequent infusion services. In addition, certain cancer patients may not be eligible for intravenous formulation due to limited vein access caused by long-term and numerous drug treatments. Moreover, intravenous formulation of macromolecule can cause a high plasma-drug concentration, which, although lasting a short period, can increase the risk of infusion-related reactions.

Subcutaneous formulation is currently not available for PD-(L)1 inhibitors due to difficulties in formulation development. For subcutaneous formulation, the volume for each injection is typically under 2ml, because otherwise patients may experience absorption issues and require auxiliary medication. In order to achieve a safe subcutaneous administration, the concentration of PD-(L)1 inhibitors should ideally be over 150.0 mg/ml, which is technically challenging. In addition, the subcutaneous formulation of macromolecule drugs generally result in relatively low bioavailability.

Advantages of KN035

Benefitting from the sdAb format, KN035 has half the molecular weight as compared to a full antibody with better stability and high solubility, which enables the development of high concentration formulation injections suitable for subcutaneous injection. As a result, compared with approved PD-(L)1 inhibitors, our KN035 potentially has the following advantages:

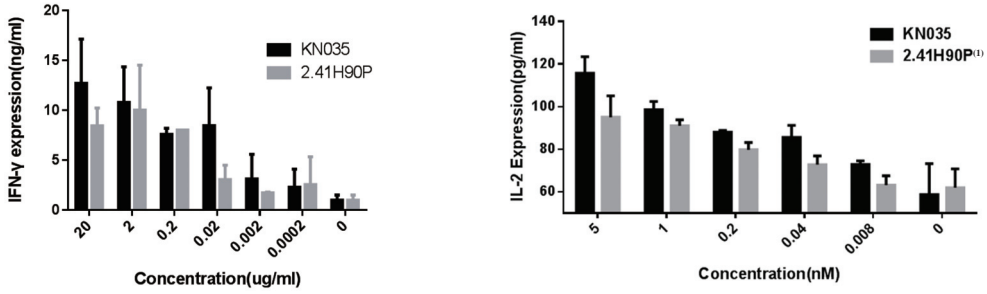
- *Better patient compliance with increased convenience*. Subcutaneous formulation enables quicker administration and self-injection, which is more convenient for patients in long-term care and enables better patient compliance with the treatment regimen;

- *Wider patient coverage*. Our KN035 could be used in patients who are not eligible for intravenous administration, such as elderly patients who are vulnerable to complications of intravenous fluid overload, patients who are heavily treated with chemotherapy resulting in vein shrinkage, and NSCLC/ESCC patients who are not suitable for intravenous administration shortly after radiotherapy; and

- *Relatively stable plasma-drug concentration*. The plasma-drug concentration of KN035 is relatively stable without significant fluctuations due to the nature of subcutaneous administration. Its different PK profile compared with intravenous formulation may lower risks to patients.

In addition, in pre-clinical studies, we compared our KN035 with durvalumab, the only approved PD-L1 inhibitor at the time, and KN035 showed the following potential advantages:

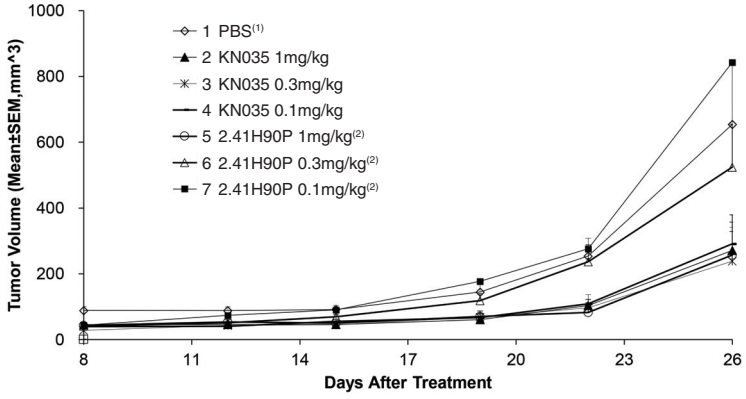
- *Stronger T-cell activation effect.* The level of T-cell activation can be measured by the secretion levels of IFN-γ and IL-2. Higher secretion levels are generally associated with stronger T-cell activation. In pre-clinical studies, our KN035 had a better stimulatory effect on IFN-γ and IL-2 secretion compared to durvalumab. See "—Pre-clinical Studies—^{89}Zr-KN035 Tumor Targeting and Biological Distribution in Tumor-bearing Mice." The following graphs illustrate the secretion levels of IFN-γ and IL-2 stimulated by KN035 and durvalumab.



(1) 2.41H90P was an in-house produced durvalumab with the same amino acid sequence as MedImmune's Imfinzi (durvalumab), and cloned using the 2.14H9 method.

Source: Investigator's Brochure (v.4.0) on KN035

- *Higher anti-tumor efficacy.* Each of KN035 and durvalumab was injected intraperitoneally in mice at 0.1 mg/kg, 0.3 mg/kg and 1.0 mg/kg dose levels. As illustrated in the following graph, our KN035 drug candidate showed stronger tumor growth inhibition effects than that of durvalumab at 0.3 mg/kg and 0.1 mg/kg.



(1) The control group was given PBS alone.

(2) 2.41H90P was an in-house produced durvalumab with the same amino acid sequence as MedImmune's Imfinzi (durvalumab), and cloned using the 2.14H9 method.

Source: Investigator's Brochure (v.4.0) on KN035

- *Quicker tumor penetration*. After injection of KN035 and durvalumab in tumor-bearing nude mice, tumor radioactivity signal was consistently higher in the KN035 group than the durvalumab group up to 52 hours post injection. The tumor radioactivity signal in the KN035 group at 1 hour and 2.5 hours was statistically significantly higher than that of durvalumab, which translates to potentially better biological distribution of KN035. See "—Pre-clinical Studies—^{89}Zr-KN035 Tumor Targeting and Biological Distribution in Tumor-bearing Mice."

Pre-clinical Studies

^{89}Zr-KN035 Tumor Targeting and Biological Distribution in Tumor-bearing Mice

The aim of this study was to investigate the *in vivo* bio-distributions of ^{89}Zr-KN035 and ^{89}Zr-durvalumab in melanoma-xenografted mouse models. A375-hPD-L1 was inoculated into mice subcutaneously. When the tumor size was larger than 100 mm^3, ^{89}Zr-KN035 (10.0 mg/kg) was injected through the tail vein into the transformed mice. At various time points post injection, whole body CT/MRI scans were performed on the mice, and the scan data were analyzed and used to calculate the uptake values of the radioactive material in each region of interest (ROI) on the mice. The tumor, heart, liver, kidney, brain and other organs were considered as ROI, and the distribution of ^{89}Zr-labeled durvalumab was also investigated side by side with KN035 for comparison. The injection amount of durvalumab was 18.4 mg/kg, the same molar amount as KN035. The results showed that following the injection of ^{89}Zr-KN035 and ^{89}Zr-durvalumab, the uptake value of radioactive material by the tumor increased. At all measured time points between 1 to 52 hours, the radioactive signals were higher in the KN035 group than in the durvalumab group, and the signals showed a significant difference between 1 to 2.5 hours. See "—Advantages of KN035—Quicker tumor penetration." We also have done other pre-clinical studies to evaluate safety and efficacy profiles of KN035, and KN035 exhibited comparable results to durvalumab.

Summary of Clinical Results

Phase I Dose Escalation Clinical Trial in China

An open-label, single-arm phase I dose escalation clinical trial of our KN035 has been completed in China. The safety and efficacy data of this trial was presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in June 2019. Based on the data presented in the ASCO Annual Meeting ("**ASCO Presentation**"), 17 subjects were enrolled in this trial as of May 1, 2019.

Study purpose. The primary objectives of the phase I dose escalation clinical trial were to assess safety and tolerability profile and MTD of single agent KN035 administered subcutaneously in subjects with advanced solid tumors. The secondary objectives were to evaluate the PK profile, immunogenicity and the anti-tumor activities.

Study design. This trial adopted a modified "3+3" design with a DLT evaluation period of 28 days. Subjects received KN035 in six cohorts at 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg, 2.5 mg/kg, 5.0 mg/kg and 10.0 mg/kg QW subcutaneously. One patient was planned for the 0.1 and 0.3 mg/kg cohorts in absence of treatment-related grade 2 AE. Starting from the 1.0 mg/kg cohort, a traditional "3+3" design was followed. Safety and tolerability would be assessed by monitoring TEAEs. Tumor assessments would be performed based on RECIST version 1.1.

Safety. According to the ASCO Presentation, 17 subjects were enrolled across all the six dose levels as of May 1, 2019. The majority of the subjects received two or more prior systemic oncology treatment. According to the ASCO Presentation, 16 of the subjects had discontinued treatment due to disease progression (n=15) or consent withdrawal (n=1). All of the enrolled subjects experienced TEAEs. 13 (76.5%) experienced treatment-related TEAEs. Three (17.6%) subjects experienced serious TEAEs, although none were determined to be treatment-related. One TEAE led to treatment discontinuation of three subjects but was also determined to be not treatment-related. No DLT was reported and MTD was not reached. Details of the TEAEs observed from the 17 subjects enrolled in the phase I dose escalation study are summarized in the following table.

TEAE categories[(1)]	**n (%) (N=17)**
AE	17 (100%)
Any TEAE	17 (100%)
TEAE, Grade ≥ 3	7 (41.2%)
Treatment-related TEAE[(2)]	13 (76.5%)
Treatment-related TEAE, Grade ≥ 3[(3)]	1 (5.9%)
SAEs	3 (17.6%)
Treatment-related SAEs	0
IrAEs	1 (5.9%)
IrAEs, Grade ≥ 3[(3)]	1 (5.9%)
TEAE leading to permanent treatment discontinuation	1 (5.9%)
Treatment-related TEAE leading to permanent treatment discontinuation	0
TEAE leading to death	0
Treatment-related TEAE leading to death	0

(1) Reported under National Cancer Institute Common Terminology Criteria for Adverse Events v. 4.03.

(2) The most frequent treatment-related TEAEs (all grades ≥ 10%) included increased alanine aminotransferase (n=6, 35.3%), increased aspartate aminotransferase (n=6, 35.3%), dermatitis/rash (n=3, 17.6%), blood bilirubin increased (n=3, 17.6%), injection site reaction (n=2, 11.8%).

(3) An immune-related dermatitis that occurred in the 0.3 mg/kg cohort. The subject recovered completely after the study drug was withheld.

Source: Phase I Study of KN035, the First Subcutaneous Administered, Novel Fusion Anti-PD-L1 Antibody in Patients with Advanced Solid Tumors in China, Abstract No. 2608, Poster No. 252, 2019 American Society of Clinical Oncology (ASCO) Annual Meeting

Efficacy. According to the ASCO Presentation, 15 out of 17 subjects were evaluable patients for the efficacy analysis. Three subjects had confirmed PR, including one RCC subject in the 2.5 mg/kg cohort, one intrahepatic cholangiocarcinoma subject from the 5.0 mg/kg cohort and one BTC subject from the 10.0 mg/kg cohort. In addition, five subjects achieved SD. All 15 subjects completed at least one post-baseline tumor assessments, according to the ASCO Presentation. Two enrolled subjects who had not reached the first post-baseline tumor assessment were excluded.

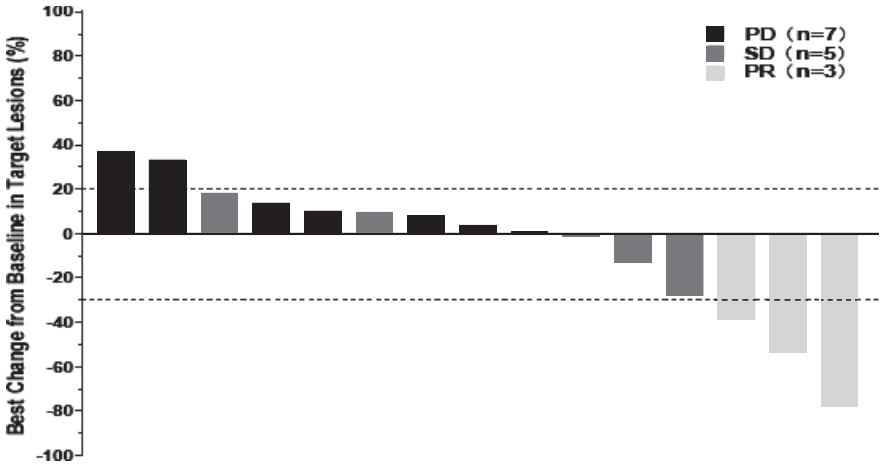
The table below summarizes the best overall response in the efficacy analysis of this trial, according to the ASCO Presentation.

Response	0.1 mg/kg (N=1)	0.3 mg/kg (N=2)	1.0 mg/kg (N=3)	2.5 mg/kg (N=3)	5.0 mg/kg (N=3)	10.0 mg/kg (N=3)	Total (N=15)
				n (%)			
CR	0	0	0	0	0	0	0
PR	0	0	0	1	1	1	3 (20.0%)
SD	0	0	2	2	1	0	5 (33.3%)
PD	1	2	1	0	1	2	7 (46.7%)
CR+PR	0	0	0	1	1	1	3 (20.0%)
DCR (CR+PR+SD)	0	0	2	3	2	1	8 (53.3%)

Abbreviations: CR=complete response, PR=partial response, SD=stable disease, PD=progressive disease, DCR=disease control rate.

Source: Phase I Study of KN035, the First Subcutaneous Administered, Novel Fusion Anti-PD-L1 Antibody in Patients with Advanced Solid Tumors in China, 2019 American Society of Clinical Oncology (ASCO) Annual Meeting

The following waterfall plot shows the best overall response of the 15 evaluable subjects receiving KN035 as measured by percentage of change of target lesions from baseline.



Abbreviations: PD=progressive disease, SD=stable disease, PR=partial response.

Source: Phase I Study of KN035, the First Subcutaneous Administered, Novel Fusion Anti-PD-L1 Antibody in Patients with Advanced Solid Tumors in China, 2019 American Society of Clinical Oncology (ASCO) Annual Meeting

Conclusion. According to the ASCO Presentation, KN035 exhibited a tolerable safety profile and preliminary efficacy in patients with advanced malignancies. Based on these results, it is believed that further clinical development of our KN035 is warranted.

Phase I Dose Escalation Clinical Trial in the United States

An open-label, single-arm phase I dose escalation clinical trial of our KN035 has been completed in the United States. The safety and efficacy data of this trial was presented at the 2018 Annual Congress of the European Society for Medical Oncology (ESMO) in October 2018. Based on the data presented in the ESMO (the "**ESMO Presentation**"), 18 subjects were enrolled in this trial as of July 5, 2018.

Study purpose. The primary objectives of the phase I dose escalation clinical trial were to evaluate and characterize the tolerability and safety profile of single agent KN035 in subjects with locally advanced or metastatic solid tumors. The secondary objectives were to characterize the PK profile, determine MTD and to evaluate the anti-tumor activities.

Study design. This trial adopted a modified "3+3" design with the DLT evaluation period of 28 days. Subjects received KN035 across eight cohorts at 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg, 2.5 mg/kg, 5.0 mg/kg and 10.0 mg/kg QW subcutaneously. One patient was planned for the 0.01, 0.03 and 0.1 mg/kg cohorts in absence of treatment-related grade 2 AE. Starting from the 0.3 mg/kg cohort, traditional "3+3" design was followed. Safety and tolerability would be assessed by monitoring TEAEs. Tumor assessments would be performed based on RECIST version 1.1.

Safety. According to the ESMO Presentation, 18 subjects with various types of solid tumors were enrolled across all eight dose levels as of July 5, 2018. The median duration of exposure to KN035 was 9 weeks with a range of 6 to 32 weeks. As of the same date, two of the subjects (11.1%) remained in the study, 11 subjects had discontinued treatment due to disease progression, three subjects had discontinued treatment due to TEAEs, and two subjects had discontinued treatment due to the opinion of the investigator that no more clinical benefit could be obtained or other reasons. All of the 18 enrolled subjects experienced TEAEs. Treatment-related TEAEs at grade 3 or above include increased aspartate aminotransferase (10.5%), increased alanine aminotransferase (10.5%) and lymphopenia (10.5%). No DLT was observed and the planned maximum dose of 10.0 mg/kg has been reached.

Efficacy. According to the ESMO Presentation, 17 out of 18 subjects were evaluable patients for the efficacy analysis. Two subjects had confirmed PR, including one NSCLC subject from the 0.3 mg/kg QW cohort (response duration of 9 months) and one MSI-H prostate cancer subject from the 2.5 mg/kg QW cohort (ongoing duration of 10 months). In addition, five subjects had achieved SD. All 17 evaluable subjects had completed one post-baseline tumor assessments according to the ESMO Presentation. One enrolled subject who had not reached the first post-baseline tumor assessment was excluded. The table below summarizes the best overall response in the efficacy analysis of this trial according to the ESMO Presentation.

	0.01 mg/kg weekly (N=1)	0.03 mg/kg weekly (N=1)	0.1 mg/kg weekly (N=1)	0.3 mg/kg weekly (N=3)	1.0 mg/kg weekly (N=3)	2.5 mg/kg weekly (N=3)	5.0 mg/kg weekly (N=3)	10.0 mg/kg weekly (N=3)	Total (N=18)
	n (%)	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*
CR	0	0	0	0	0	0	0	0	0
PR	0	0	0	1 (33.3)	0	1 (33.3)	0	0	2 (11.1)
SD	0	1 (100)	0	1 (33.3)	1 (33.3)	0	1 (33.3)	1 (33.3)	5 (27.8)
PD	1 (100)	0	1 (100)	0	2 (66.7)	2 (66.7)	2 (66.7)	1 (33.3)	9 (50.0)
NE	0	0	0	0	0	0	0	1 (33.3)	1 (5.6)
CR+PR	0	0	0	1 (33.3)	0	1 (33.3)	0	0	2 (11.1)
DCR: (CR+PR+SD)	0	1 (100)	0	2 (66.7)	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)	7 (38.9)

Abbreviations: CR=complete response, PR=partial response, SD=stable disease, PD=progressive disease, NE=not evaluable, DCR=disease control rate.

Source: *Phase I Study of KN035, A Novel Fusion Anti-PD-L1 Antibody Administered Subcutaneously in Patients with Advanced Solid Tumors in the USA, 2018 Annual Congress of the European Society for Medical Oncology (ESMO)*

PK profile. This study showed that the exposure to KN035 was dose-dependent and increased proportionally across all eight dose levels. Average half-life (t1/2) of KN035 was approximately 200 hours.

Conclusion. According to the ESMO Presentation, KN035 exhibited a favorable safety profile in subjects with advanced solid tumors and preliminary efficacy results demonstrated encouraging anti-tumor activities.

Phase I Clinical Trial in Japan

An open-label phase I clinical trial of KN035 is being conducted in Japan. The safety, efficacy and PK data of this trial as of the May 5, 2019 was presented at 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in June 2019. Based on the data presented in the ASCO Annual Meeting (the "**Japan Trial ASCO Presentation**"), 26 subjects were enrolled in this trial as of May 5, 2019.

Study purpose. The primary objectives of the phase I clinical trial were to assess safety and tolerability profile of single agent KN035 in Japanese subjects with previously treated advanced solid tumors. The secondary objectives were to characterize the PK profile, determine MTD and to evaluate the anti-tumor activities.

Study design. This phase I trial consisted of a multi-dose escalation phase followed by a dose expansion phase. Subjects received KN035 across five cohorts at 1.0 mg/kg, 2.5 mg/kg and 5.0 mg/kg QW subcutaneously, and 2.5 mg/kg and 5.0 mg/kg Q2W subcutaneously. The QW schedule adopted a traditional "3+3" design. For the Q2W schedule, six patients were planned for each cohort. Safety and tolerability would be assessed by monitoring TEAEs under CTCAE v. 4.0. Tumor assessments would be performed based on RECIST version 1.1. Full PK sampling was performed after the first dose of cycle 1 (28 days) and sparse PK samples were collected at pre-dose and around C_{max} during the subsequent cycles.

Safety. According to the Japan Trial ASCO Presentation, 26 subjects were enrolled across five dose levels as of May 5, 2019. No MTD was reached. As of the same date, three subjects had remained in the study. 21 subjects had discontinued treatment due to disease progression and two subjects had discontinued treatment due to TEAE. All of the enrolled subjects experienced TEAEs, 17 subjects (65.4%) experienced treatment-related TEAEs, and only one grade 3 treatment-related TEAE (cerebral infraction) was reported. There were no grade 4/5 treatment-related TEAEs. There were a total of four SAEs, and two were treatment-related SAEs. No DLT was reported.

Efficacy. According to the Japan Trial ASCO Presentation, nine out of 26 subjects were evaluable patients for the efficacy analysis. Two subjects had confirmed PR and subjects had unconfirmed PR. The other five evaluable subjects had achieved SD. 17 enrolled subjects who had not reached the first post-baseline tumor assessment were excluded.

PK profile. In the dose escalation phase, the exposure to KN035 was dose-dependent and increased proportionally. T_{max} varied from 96 to 168 hours after a single dose as shown in Figure 1 below. In the dose expansion phase, the exposure to KN035 was dose-dependent and increased proportionally. T_{max} varied from 96 to 120 hours after a single dose as shown in Figure 2 below. Preliminary PK suggested a prolonged half-life that would support a less frequent dosing schedule.

Figure 1: Pharmacokinetics (Escalation Part)

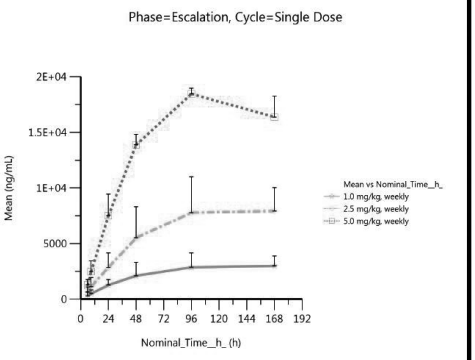
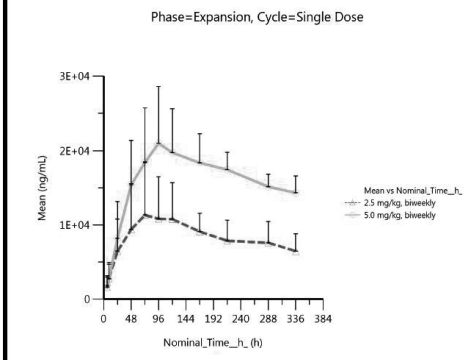


Figure 2 : Pharmacokinetics (Expansion Part)



Source: Phase I Study and Pharmacokinetic Study of KN035, the First Subcutaneous Administered, Novel Fusion Anti-PD-L1 Antibody in Japanese Patients with Advanced Solid Tumors, 2019 American Society of Clinical Oncology (ASCO) Annual Meeting

Conclusion. KN035 exhibited a favorable safety profile in patients with advanced malignancies and preliminary efficacy results demonstrated promising anti-tumor activities.

Clinical Trial Development Plan

We collaborate with 3DMed on a broad development program targeting a number of strategically selected indications in China, the United States, Japan and other countries, to support regulatory submissions for multiple indications both in China and other countries. Under the Co-development Agreements, 3DMed is responsible for the clinical trials and commercialization of KN035. 3DMed led the formulation of the clinical trial plan for KN035 and selected non-PRC jurisdictions, including the U.S. and Japan, based on its commercialization strategy. Japan and the United States are members of the ICH. A multi-regional clinical trial conducted in ICH member countries is expected to lower operational costs in light of the consistency of general rule requirements. Moreover, the subjects in clinical trials conducted in Japan and China are of East Asian ethnicity, and therefore clinical trial data from one country could be leveraged to support clinical trials and accelerate the clinical development process in the other country. The clinical trials carried out by 3DMed include: (i) phase I clinical trials in China of KN035 as a first-line monotherapy for advanced solid tumors and HCC, (ii) an exploratory phase II clinical trial in China of KN035 as a first-line therapy in combination with chemotherapy for gastric cancer, (iii) a phase III clinical trial of KN035 in China as a first-line therapy in combination with chemotherapy for BTC, (iv) a phase II pivotal clinical trial of KN035 in China as a second-line or later-line monotherapy for MSI-H colorectal carcinoma tumors and dMMR non-colorectal cancers, (v) a phase I clinical trial of KN035 in the United States as a monotherapy for locally advanced or metastatic solid tumors, and (vi) a phase I clinical trial of KN035 in Japan as a monotherapy for advanced solid tumors. The first BLA for KN035 is expected to be filed by the end of 2020 for dMMR/MSI-H solid tumors.

Competition

As of the Latest Practicable Date, there were a total of six PD-(L)1 inhibitors in the global market outside China, of which three target PD-1 and three target PD-L1. As of the same date, five PD-1 inhibitors were approved in China and no PD-L1 inhibitor was available. As of August 31, 2019, there were 21 PD-(L)1 inhibitor candidates registered with the NMPA, of which there were two at BLA stage and ten in phase III clinical trials. As of the same date, there were eight PD-(L)1 inhibitor candidates in phase III clinical trials in the United States. The following table sets out details of approved PD-(L)1 inhibitors in China and the United States as of August 31, 2019.

Trade name (Generic name)	Company	Immune checkpoint	Number of indications	Indications	Treatment line	Date of approval
PRC						
Opdivo (nivolumab)	BMS	PD-1	1	EGFR/ALK negative locally advanced or metastatic NSCLC	2L	Jun-2018
Keytruda (pembrolizumab)	Merck	PD-1	2	Unresectable or metastatic melanoma	2L	Jun-2018
				EGFR/ALK negative metastatic non-squamous non-small cell lung cancer	1L (with chemo)	Mar-2019
Tuoyi (toripalimab)	Junshi	PD-1	1	Unresectable, metastatic malignant melanoma	≥2L	Dec-2018
Tyvyt (sintilimab)	Innovent	PD-1	1	Refractory Hodgkin's lymphoma	3L	Dec-2018
Ailituo (camrelizumab)	Hengrui	PD-1	1	Refractory Hodgkin's lymphoma	3L	May-2019
U.S.						
Opdivo (nivolumab)	BMS	PD-1	9	Unresectable or metastatic melanoma	2L	Dec-2014
				Metastatic non-small cell lung cancer	2L	Oct-2015
				Advanced renal cell carcinoma	2L	Nov-2015
				Classical Hodgkin lymphoma	≥3L	May-2016
				Recurrent or metastatic squamous cell carcinoma of the head and neck	2L	Nov-2016
				Locally advanced or metastatic urothelial carcinoma	2L	Feb-2017
				MSI-H or dMMR metastatic colorectal cancer	2L	Aug-2017
				Hepatocellular carcinoma	2L	Sep-2017
				Metastatic small cell lung cancer	3L	Aug-2018
Keytruda (pembrolizumab)	Merck	PD-1	13	Unresectable or metastatic melanoma	1L	Sep-2014
				Metastatic NSCLC	1L (mono or with chemo)	Oct-2015
				Recurrent or metastatic HNSCC	1L	Aug-2016
				Refractory cHL	≥3L	Mar-2017

Trade name (Generic name)	Company	Immune checkpoint	Number of indications	Indications	Treatment line	Date of approval
				Locally advanced or metastatic urothelial carcinoma	2L	May-2017
				Unresectable or metastatic, MSI-H or dMMR solid tumors or colorectal cancer	≥3L	May-2017
				Recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma	≥3L	Sep-2017
				Refractory PMBCL	3L	Jun-2018
				Recurrent or metastatic cervical cancer	1L	Jun-2018
				Hepatocellular carcinoma	2L	Nov-2018
				Locally advanced or metastatic Merkel cell carcinoma	1L	Dec-2018
				Adjuvant treatment melanoma with involvement of lymph node(s)	adjuvant	Feb-2019
				Advanced RCC	1L (with Axitinib)	Apr-2019
				Metastatic SCLC	>2L	Jun-2019
				Recurrent locally advanced or metastatic squamous cell carcinoma (esophageal cancer)	>2L	Jul-2019
Libtayo (cemiplimab)	Regeneron Pharmaceuticals, Inc./Sanofi S.A.	PD-1	1	Locally advanced or metastatic CSCC	2L	Sep-2018
Tecentriq (atezolizumab)	Roche/ Genentech	PD-L1	5	Locally advanced or metastatic urothelial carcinoma	2L	May-2016
				Metastatic non-small cell lung cancer	2L	Oct-2016
				EGFR/ALK negative metastatic non-squamous non-small cell lung cancer	1L (with Bevacizumab)	Dec-2018
				Locally advanced or metastatic triple-negative breast cancer	1L (with chemo)	Mar-2019
				Extensive-stage small cell lung cancer	1L (with chemo)	Mar-2019
Bavencio (avelumab)	Merck KGaA/Pfizer	PD-L1	3	Metastatic Merkel cell carcinoma	2L	Mar-2017
				Locally advanced or metastatic urothelial carcinoma	2L	May-2017
				Advanced renal cell carcinoma	1L (with chemo)	May-2019
Imfinzi (durvalumab)	AstraZeneca/ MedImmune	PD-L1	2	Locally advanced or metastatic urothelial carcinoma	2L	May-2017
				Unresectable, Stage III non-small cell lung cancer	2L	Feb-2018

Abbreviations: 1L = first-line; 2L = second-line, 3L = third-line; mono = monotherapy, chemo = chemotherapy, NSCLC = non-small cell lung cancer, RCC = renal cell carcinoma, EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma kinase, MSI-H = high microsatellite instability, dMMR = DNA mismatch repair, CSCC = cutaneous squamous cell carcinoma, PMBCL = primary mediastinal large B-cell lymphoma, cHL = classical hodgkin lymphoma, HNSCC = head and neck squamous cell carcinoma.

Source: NMPA; FDA; CIC Report (as of August 31, 2019)

Among all of the approved PD-(L)1 inhibitors or drug candidates in China, our KN035 is the only one that can be subcutaneously administered, which is a more convenient administration form for patients that enables improved patient compliance and wider patient coverage. In addition, with the indication for dMMR/MSI-H solid tumors, our KN035 is potentially the first pan-cancer PD-L1 inhibitor to be approved in China. We believe KN035 has the potential to be the first PD-(L)1 inhibitor to be approved for BTC in China.

Material Communications

KN035 obtained IND approval for oncology treatment from the NMPA, the FDA and the Pharmaceuticals and Medical Devices Agency in Japan in December 2016, November 2016 and May 2017, respectively. In preparation the relevant IND filings, we are working with 3DMed on communications with relevant authorities about KN035 and did not have material communications with the relevant authorities. To date, none of these authorities have raised any objections or material concerns with respect to the development of KN035.

OUR COLLABORATION ARRANGEMENTS

Co-development Agreements with 3DMed

In February 2016, we entered into the initial Co-development Agreement with 3DMed for KN035.

Under the Co-development Agreements, we agree to co-own the patent rights under a PCT application and its multiple national phase applications (including the ones in China and the United States) covering the molecule of KN035 with 3DMed (the "**Patent Rights**"). 3DMed's ownership interests to the Patent Rights is limited to oncology treatment and can only be used for KN035 or drugs using KN035 as a component, excluding BsAbs, multi-functional antibodies, fusion proteins and other derivative antibodies.

Under the Co-development Agreements, we are responsible for, among other things, completing CMC studies and pre-clinical studies and manufacturing KN035 samples for clinical trials at our own cost, while 3DMed is responsible for, among other things, designing, conducting and monitoring clinical trials and trial data, reviewing registration filings, and conducting global commercialization of KN035 at its own cost. 3DMed is entitled to obtain the new drug certificate and would have exclusive commercialization rights for KN035 worldwide. We jointly prepared IND documents and expect to jointly prepare BLA documents for KN035. We are entitled to apply for and obtain the GMP certificate to manufacture KN035. We own the rights to manufacture and supply KN035 to 3DMed. During the clinical stage, we will supply KN035 drug samples for free. After KN035 enters the commercialization stage, we will supply KN035 to 3DMed on a cost-plus basis.

Under the Co-development Agreements, we were eligible to receive an upfront payment of RMB10 million, which had been paid as of the Latest Practicable Date and was recognized as contract liabilities in our consolidated balance sheet. See "Financial Information—Description of Certain Consolidated Statement of Financial Position Items—Contract Liabilities." Our ownership in KN035 is adjusted based on achievement of certain milestones. Upon the signing of the Co-development Agreements and receipt of the upfront payment, we owned a 90% interest in KN035 and 3DMed owned the remaining 10% interest in KN035. Upon KN035 receiving approval for oncology treatment from the NMPA or the FDA, we would be entitled to 49% interest in KN035, and 3DMed would own a 51% interest in KN035. Upon the approval and commercialization of KN035, we would be entitled to 49% of the profit before tax generated from the sales of KN035 in China, and based on 3DMed's cost control performance as agreed under the Co-development Agreements, the profit before tax allocation would be further adjusted among both parties. We would not bear the operating losses, if any, caused by the commercialization of KN035.

The Co-development Agreements can be terminated in the following situations: (i) if a contracting party breaches the agreements, (ii) if the obligations under the Co-development Agreements cannot be performed due to force majeure, or (iii) if a party fails to perform its obligations related to the intellectual property rights.

Collaboration Agreement with Sunshine Lake

In January 2019, we entered into a collaboration agreement (the "**Sunshine Lake Agreement**") to jointly develop an anti-tumor combination therapy (the "**Anti-tumor Combination Therapy**") with Sunshine Lake. Under the Sunshine Lake Agreement, both parties have agreed to cooperate in the development, manufacturing and commercialization of the Anti-tumor Combination Therapy indicated for human HCC in China based on two drug candidates, namely Sunshine Lake's CT-053 (an anti-tumor small-molecule drug candidate at clinical stage) and our KN046. In accordance with the Sunshine Lake Agreement, we and Sunshine Lake have established a joint steering committee with equal representation from each party to coordinate, oversee and make decisions in relation to the development, commercialization and manufacturing of the Anti-tumor Combination Therapy globally.

The collaboration consists of two stages. The first stage started from the effective date of the Sunshine Lake Agreement and continues to the completion date of the phase I clinical trial of the Anti-tumor Combination Therapy. The second stage starts after the first stage and ends at the end of 15 years after any BLA approval of the Anti-tumor Combination Therapy. Under the Sunshine Lake Agreement, for the first stage, both parties are jointly responsible for applying for the IND approval, formulating clinical plans and conducting phase I clinical trials of the Anti-tumor Combination Therapy. Sunshine Lake is generally responsible for all research and development prior to the phase II clinical trial. The manner of collaboration for phase II and phase III clinical trials will depend on then-available clinical results, and the allocation of responsibilities for research and development during the phase II and phase III clinical trials between both parties will be determined by supplemental agreements.

Under the Sunshine Lake Agreement, both parties are jointly responsible for registration regulatory filings and commercialization of the Anti-tumor Combination Therapy. The allocation of sales revenue at commercialization stage will be determined based on the allocation of research and development expenses incurred during clinical trials of the Anti-tumor Combination Therapy.

In addition, each party is responsible for the supply of its own drug at its own cost, and each party can only use the other party's drug solely for the purpose of developing the Anti-tumor Combination Therapy. The information and data (including drug safety data) from the phase I clinical trial will be owned by Sunshine Lake, and we will have free access to such information and data. The ownership of information and data (including drug safety data) after phase I will be determined by supplemental agreements. Each party maintains ownership of intellectual property rights in its own drug candidate. Both parties will jointly own the right to out-license the Anti-tumor Combination Therapy, if such therapy approved.

Neither party is obligated to pay upfront payments, milestone payments, or royalty fees under this agreement. We did not make or receive any payment pursuant to the Sunshine Lake Agreement during the Track Record Period.

The term of this agreement is from the effective date of the Sunshine Lake Agreement and will terminate fifteen years after the BLA for the Anti-tumor Combination Therapy is approved. The Sunshine Lake Agreement can be terminated (i) by mutual consent, (ii) in the event of a material breach or insolvency, or (iii) by the occurrence of a force majeure event.

Non-exclusive Licensing Agreements with Suzhou Dingfu

Suzhou Dingfu is primarily engaged in the research and development of immunotherapy antibody drugs, and was held as to 70% by Suzhou Alphamab and 30% by Mr. Fu Yang-Xin, an Independent Third Party, at the time of its establishment. After its registered capital increase in September 2016, Suzhou Dingfu was held by Suzhou Alphamab, Mr. Xue Chuanxiao (薛傳校), Mr. ZHANG Xitian (張喜田) and Mr. Fu Yang-Xin as to 37%, 16.5%, 16.5% and 15%, respectively. Dr. Xu also held 15% of the equity interests in Suzhou Dingfu as a nominee for and on behalf of certain employees of Suzhou Dingfu under an employee incentive scheme from September 2016 and were later transferred to Mr. ZHANG Xitian in September 2018. Upon completion of such transfer and other equity interest transfers among the shareholders of Suzhou Dingfu, the considerations of which were determined with reference to the price proposed by other potential third party buyers, Suzhou Dingfu is held as to 50% by Mr. ZHANG Xitian and 50% by Mr. Xue Chuanxiao, respectively, each of whom is an angel investor of Suzhou Alphamab. Suzhou Dingfu has a product pipeline with over 15 candidates including monoclonal antibodies, fusion proteins and diagnostic reagent. The unaudited revenue of Suzhou Dingfu for the year ended December 31, 2018 was approximately RMB5.6 million, and net loss was approximately RMB27.5 million. Its unaudited total asset was approximately RMB9.4 million and net asset value was approximately RMB8.8 million as of December 31, 2018. Dr. Xu and Ms. Liu Yang previously held certain positions in Suzhou Dingfu. Please see "Directors and Senior Management—Board of Directors—Executive Directors" for details.

In April 2016, Suzhou Alphamab and Suzhou Dingfu entered into a non-exclusive licensing agreement (together with the supplemental agreements entered into in March 2018 and in March 2019, the "**Non-exclusive Licensing Agreement**"). In March 2018, Suzhou Alphamab and Suzhou Dingfu also entered into a patent implementation and licensing agreement (together with the supplemental agreement entered into in February 2019, the "**Patent Implementation and Licensing Agreement**"). We became a party to the Non-exclusive Licensing Agreement and the Patent Implementation and Licensing Agreement pursuant to the supplemental agreements entered into in March 2019 and February 2019, respectively.

Under the Non-exclusive Licensing Agreement, Suzhou Dingfu has granted a non-exclusive, royalty-free license for a DF004 full human antibody patent to us to research, develop, manufacture and commercialize a DF004/PD-L1 bispecific antibody drug and a DF004/CTLA-4 bispecific antibody drug. Suzhou Alphamab and we jointly granted a non-exclusive, royalty-free license for a CTLA-4 humanized antibody patent to Suzhou Dingfu to research, develop, manufacture and commercialize a DF003/CTLA-4 bispecific antibody drug. The agreement will be terminated upon expiration date of each patent.

Under the Patent Implementation and Licensing Agreement, we granted a non-exclusive license for a CRIB platform patent to Suzhou Dingfu to research, develop, manufacture and commercialize a tumor-targeting cytokine drug for oncology treatment. If Suzhou Dingfu commercializes any product developed under the Patent Implementation and Licensing Agreement, Suzhou Dingfu will pay us an amount equal to a low single digit percentage of net sales. If Suzhou Dingfu sells and transfers these products to a non-wholly owned subsidiary, Suzhou Dingfu will pay us an amount equal to a low double digit percentage of the consideration of the sale. If Suzhou Dingfu makes a capital contribution of these products to another company, Suzhou Dingfu will pay us an amount equal to a low single digit percentage of the valuation of such products. The agreement will be terminated upon expiration date of the patent.

RESEARCH AND DEVELOPMENT

Research and development is crucial to our growth. We are focused on building a leading innovative research and development platform. We conduct our research and development activities through an in-house research and development team and engage CROs from time to time to support our research and development activities. See "—Research and Development—CROs" for details. Our research and development department is divided into three teams, namely, clinical development team, drug discovery team, and regulatory team, led by Dr. Xu. As of the Latest Practicable Date, our research and development team had 68 team members, of which approximately 89.7% had bachelor's or higher degrees in biological sciences and healthcare-related fields.

Our clinical development team has two functions, namely, medical and clinical operations, and is primarily responsible for our clinical development strategy, protocol designs and study execution. Our drug discovery team is dedicated to drug discovery and pre-clinical

research. With the experience and expertise of our drug discovery team, we have successfully developed and obtained IND approvals for four drug candidates to date. In addition, we currently have four ongoing pre-clinical programs to develop bispecific antibodies for oncology treatments. We believe these drug candidates will allow us to explore additional treatment therapies and supplement our pipeline of innovative therapeutic antibodies. Early in the drug development stage, our drug discovery team will work closely with our CMC team to develop better properties for our drug candidates for a smooth process development and minimize potential issues during manufacturing. Our regulatory team is primarily responsible for our regulatory strategy, managing our regulatory filings and communicating with, and addressing questions from, regulators.

For the years ended December 31, 2017 and 2018 and the six months ended June 30, 2019, our total research and development expenses amounted to RMB53.2 million, RMB65.6 million and RMB55.8 million, respectively. We expect that our research and development expenses will increase in line with the growth of our business in the future.

Proprietary Platforms and Expertise

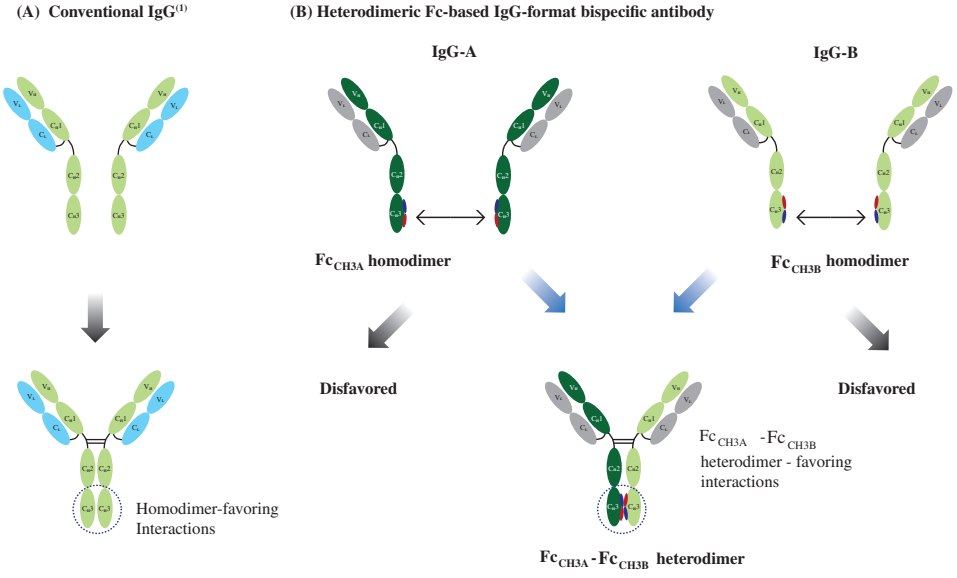
We focus on the development of technologies and platforms of antibody-based therapies for oncology treatment and our expertise in this regard. Benefitting from our proprietary protein engineering platforms and structure-guided molecular modeling expertise, we are able to develop fit-for-purpose mAbs and fusion proteins with bi-, tri- and tetra-specificity. We plan to continue to leverage these platforms and expertise to expand our biologics pipeline and develop new drug candidates, which we believe will be significant improvements to the standard of care for multiple cancer types.

CRIB Platform (Charge Repulsion Improved Bispecific Platform)

A majority of current mAbs are monospecific molecules possessing two functional binding sites for the same epitope. However, many cancers are multifactorial and mAbs with a singular specificity may not be effective in blocking other molecular pathways that lead to the survival of tumor cells. The CRIB platform is a heterodimeric Fc-based BsAb engineering platform. Bispecific mAbs are being developed with dual-targeting of receptors and/or ligands that simultaneously block multiple identified signaling pathways, thereby inducing biological effects previously unattainable with monospecific mAbs and increasing tumor-specific targeting and efficacy. While most heterodimeric Fc-based BsAb platforms primarily focus on increasing heterodimers, our platform can enable increased heterodimers and prevent formation of homodimers.

The Fc region is crucial for antibody drugs. BsAb formats without the Fc regions usually have a much shorter *in vivo* half-life, lose the ability to mediate the effector function, and may potentially affect drug manufacturing. To minimize these problems, the CRIB platform allows antibodies to retain the Fc region and its desirable biophysical properties, allowing the antibodies to be stably formulated, dosed on a convenient schedule, and have the ability to kill tumors through multiple mechanisms of action.

As illustrated in diagram A below, monospecific mAbs assemble two identical heavy chains through homodimerization interactions within the Fc region. Our CRIB platform utilizes asymmetric mutations on Fc chains to modify the charge and hydrophobic interactions and steric hindrance between the side chains of residues to assemble two different heavy chains together, while greatly disfavoring homodimerization between the same heavy chains, as illustrated in diagram B. The BsAbs generated by the CRIB platform can simultaneously bind to two different antigens as a result. Our KN026 was developed using the CRIB platform.



(1) A conventional IgG-format antibody consists of two heavy and light chains. Each heavy chain contains one variable (V_H) domain followed by a constant (C_H1) domain and two more constant (C_H2 and C_H3) domains. Each light chain contains one variable (V_L) and one constant (C_L) domain.

These designs make our CRIB platform one of the few bispecific technologies that can maintain full-length antibody properties and be optimized for industrial-scale manufacturing. The following table sets forth details of Fc-based BsAb platforms with clinically-validated drug candidates that are expected to compete with our pipeline products.

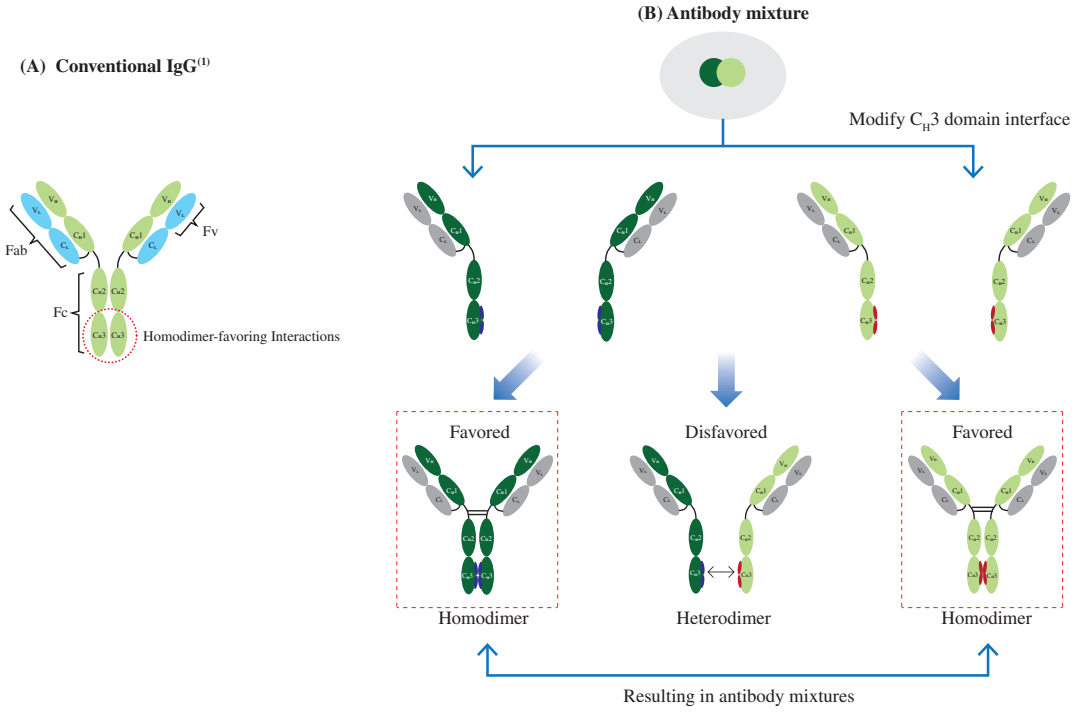
Developer	Platform	Candidate format	*In vivo* $T_{1/2}$	Representative resultant drug candidate[(1)]	Clinical validation
Glenmark Pharmaceuticals, Ltd	BEAT	Fc heterodimer	Medium/long	GBR 1302	Phase I/II
MacroGenics, Inc.	DART/ DART-Fc	Dual-affinity retargeting (DART)/ DART – Fc	Medium/long	MGD019	Phase I
Merus	Biclonics	Fc heterodimer	Medium/long	MCLA-128	Phase II
Roche	CrossMAbs/ DutaMabs	Fc heterodimer (heavy/light chain CrossMAb)	Medium/long	BTRC4017A	Phase I
Xencor, Inc.	XmAb	Fc heterodimer	Medium/long	XmAb20717	Phase I
Zymeworks	Azymetric	Fc heterodimer	Medium/long	ZW25	Phase I/II
Wuhan YZY Biopharma Co., Ltd.	YBODY	Fc heterodimer	Medium/long	M802	Phase I

(1) Each platform has at least two resultant drug candidates in clinical development. The representative resultant drug candidate refers to the one that is expected to compete with our pipeline product for oncology indication(s). There is no drug candidate near/at commercialization stage under any listed platform.

Source: CIC Report

CRAM Platform (Charge Repulsion Induced Antibody Mixture Platform)

Combinations of different antibodies have been shown to be more effective for managing certain diseases than monotherapy. Co-expression of the antibody mixture in a single cell line is key to reducing complexity during antibody development and manufacturing. Adding multiple light and heavy chains to cells can lead to production of mismatched heterodimeric by-products. To address this, in our CRAM platform, we modified the CH3 domain interface of the Fc region by changing several charge pairs to create electrostatic interactions favoring Fc homodimer formation and disfavoring Fc heterodimer formation to prevent the formation of heterodimer impurities, as shown in the diagram below.



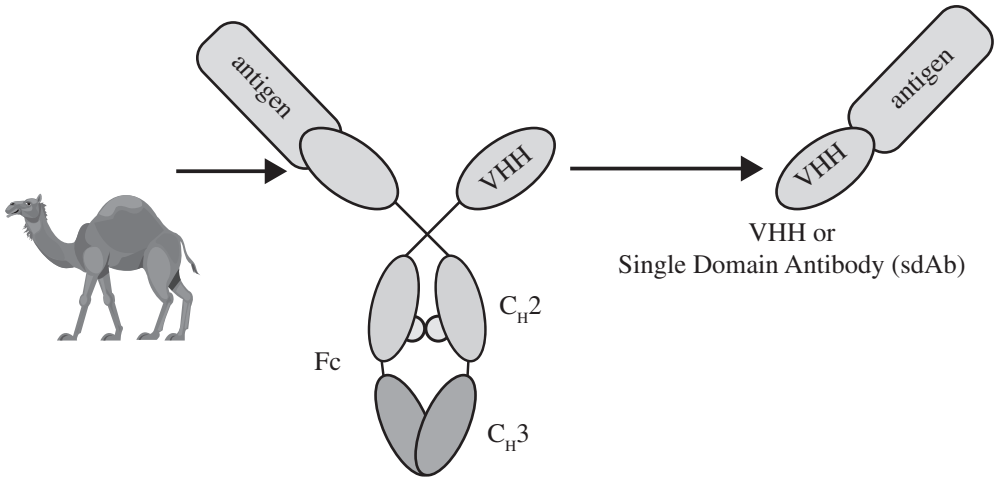
(1) A conventional IgG-format antibody consists of two heavy and light chains. Each heavy chain contains one variable (V_H) domain followed by a constant (C_H1) domain and two more constant (C_H2 and C_H3) domains. Each light chain contains one variable (V_L) and one constant (C_L) domain.

When co-expressed, these modified antibodies with altered charge polarity across the Fc dimer form homodimers that fully preserve the functions of each component. The formation of unwanted heterodimers is reduced because of designed repulsive interactions.

The CRAM platform enables a single streamlined process to produce multiple mAbs with adjustable pre-determined ratios between various mAb components, potentially lowering manufacturing and regulatory hurdles. We co-own patents for our CRAM platform in China, the U.S. and Japan. According to the CIC Report, currently in China and the U.S., our major targeted markets, there is no competing platform of our CRAM platform. In the European Union, Symphogen A/S's Sympress™ platform, which enables mAb mixture products, has resulted in a phase III-ready oncology drug candidate (Sym004) primarily indicated for mCRC.

Single Domain Antibodies Used as an Alternative Scaffold

Heavy chain-only antibodies (HCAbs) are discovered in camelid. As illustrated in the following diagram, the antigen-binding capacity of a camelid HCAb is exclusively on its variable domain of the heavy chain (VHH), which is a sdAb. The molecular weight of a full antibody is 150 to 160 kDa, and the molecular weight of a camelid HCAb is 80 to 90 kDa. A sdAb possesses fully functional antigen-binding capacity with only 12 to 15 kDa in molecular weight.



Compared with the Fab region and scFv, a sdAb is smaller and stable with a compact structure. Such properties enable sdAbs to become ideal building blocks for multifunctional biologics, with bi-, tri- or tetra-specificity.

We have developed KN046 and KN035 based on sdAb. KN046 is made of two different targeting sdAbs fused together. This allows it to have a stable and symmetrical structure with four binding moieties with a small molecular weight. KN035 is a novel fusion protein consisting of the Fc region and a sdAb. The small size makes KN035 suitable for subcutaneous formulation.

CROs

In line with industry practice, we engaged Independent Third Party CROs to provide certain services in our pre-clinical studies and clinical trials during the Track Record Period. These services primarily include performing laboratory tests and statistical analyses, conducting data collection and subject monitoring in our clinical trials, and carrying out certain studies based on our study design, which are time and labor intensive work and we believe do not require the expertise of our research and development personnel.

We have maintained stable relationships with our CROs, which we select based on various factors, including their quality, capability, reputation and research experience in the related fields. Depending on the type of service needed, we may enter into master service agreements with our CROs and separate scope of work orders for each study or trial, establishing specific and detailed working methods, procedures, standards and timelines to further ensure the quality of the outcomes. We may require periodic meetings, reports and data and analysis review as necessary.

Key terms of these agreements and scope of work orders are summarized as follows:

- *Services*. The CRO provides us with services related to pre-clinical studies and clinical trials as specified in the agreement or work order.

- *Term*. The CRO is required to complete the pre-clinical or clinical research on project basis and within the prescribed time limit.

- *Payments*. The payments are made in accordance with the payment schedule agreed by the parties.

- *Intellectual property rights*. Intellectual property arising from the pre-clinical studies and clinical trials conducted by the CROs are owned by us.

During the Track Record Period, CRO expenses were a major component of our third-party contracting costs in research and development expenses, and substantially all of our CRO expenses were attributable to our Core Product KN046, KN026, KN019 and KN035.

COMMERCIALIZATION

We plan to build our own commercialization team in China with an initial focus on late-stage drug candidates. We plan to assemble a team of personnel dedicated to medical affairs and governmental affairs in the second half of 2020 to prepare for the upcoming launch of KN046 in 2021. Our medical affairs and government affairs personnel would be primarily responsible for physician and KOL education, enhancing awareness of innovative oncology therapies, and communicating with government authorities on insurance, reimbursement and drug pricing. With a one-year lead time before we enter into the pre-launch window of our KN046, we plan to begin recruiting team leaders and sales and marketing personnel with extensive industry knowledge and biopharmaceutical marketing skills, in particular in oncology. During the pre-launch window, we plan to conduct market research and patient analysis, brand building and public education. We expect our commercialization team to have approximately 100 members in 2021. After the launch of KN046, we plan to further expand our team to actively seek insurance and reimbursement opportunities from third-party payors and government reimbursement programs to support the ongoing commercial operations of KN046 and the upcoming launch of KN026. We expect our team to cover major provinces and municipalities in China, especially the ones with relatively well-developed economies and higher levels of discretionary income. We intend to continue to expand our team in anticipation of more product launches and additional approved indications.

We are also evaluating partnership options to accelerate commercial ramp-up and maximize market potential of our assets in the U.S. market. We intend to seek partners by setting comprehensive selection criteria, primarily including commercialization teams with extensive experience in oncology drugs and our targeted indications, superior track record in commercialization partnership, favorable commercial terms, and recognition of our vision and commitment to our pipeline products. For our first product in the U.S. market, we expect to

largely leverage the partner's expertise, business network and experienced team to speed up the commercial ramp-up and gain market coverage. Meanwhile, we plan to gradually build up our own overseas commercialization capabilities and form our own team to commercialize subsequent pipeline products in the U.S. market.

Early in the formulation of our clinical plans, we took into consideration factors relating to commercialization, such as targeted patient population, competing drugs and market access. Leveraging our market analysis, we intend to develop our sales and marketing strategies during or before the pre-launch window for each near-commercial product by considering pricing, market access/reimbursement, and direct sales/distribution channels.

MANUFACTURING

Manufacturing Facilities

To date, we have not commenced manufacturing of commercial products. We currently lease a 2,235 square meter facility from Suzhou Alphamab, which houses our manufacturing and research and development facilities. See "—Properties" and "Connected Transactions—One-off Connected Transaction—Property and Equipment Lease Arrangement." This manufacturing facility is equipped with two 1,000L production lines designed and constructed to meet the NMPA and FDA's regulatory requirements and GMP standards. We are also in the process of building our own manufacturing and research and development facilities in Suzhou designed to meet NMPA and EU/FDA's cGMP requirements with an expected capacity of over 30,000L. Phase I of our new facilities is expected to be completed in late 2019 with a commercial production capacity of 4,000L (2x2,000L) and a planned GFA of 53,867 square meters. During the Track Record Period, we produced the clinical trial supply of KN035, including those used in pivotal trials, at our leased manufacturing facility. As such, we plan to continue to manufacture KN035 at this facility in the next few years and gradually transfer to our own facilities in due course. If KN035 is approved, we plan to conduct commercial production of other products in our pipeline at our own facilities.

CMC

Our CMC activities primarily include the following:

- *Process development.* Our process development involves optimizing cell culturing, protein purification and drug formulation to ensure the cost effective delivery of stable and high quality products.

- *Technology transfer.* We transfer the technology developed during pilot-scale drug production to industrial-scale production. The transfer of technologies is critical to ensuring the stability of our manufacturing process.

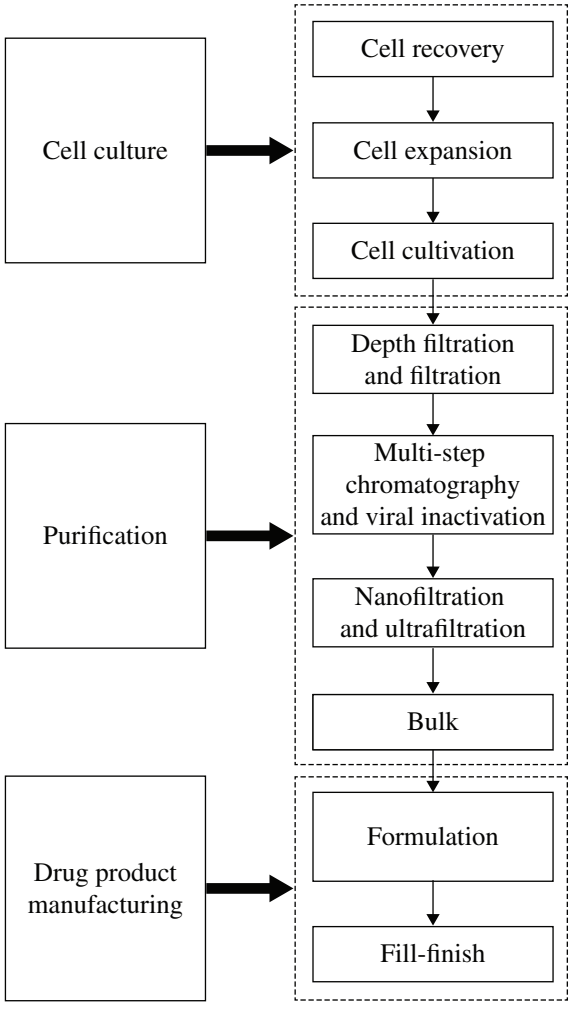
- *Process validation.* As we develop the manufacturing process, we intend to validate the process to ensure that industrial-scale production will yield consistent quality in each and every batch.

Our CMC activities also involve ensuring the consistency and quality of products manufactured in every batch through quality control tests of our raw materials and final products. We also validate the methods used in quality control to ensure that our quality control results are accurate and that we are able to detect production deficiencies. We have also established a quality assurance system to oversee and ensure that the manufacturing activities meets the GMP standards set by regulatory authorities. See "—Quality Management."

Manufacturing Process

Although our clinical-stage candidates have different biologics formats, including sdAbs, BsAbs and fusion proteins, all of them are engineered to be Fc-based with a structure similar to a native human antibody format, and therefore they can leverage generally the same antibody manufacturing process.

Our manufacturing process has three stages, namely, the cell culture stage, purification stage and drug product manufacturing stage, as set out below.



Cell Culture

The cell culture stage is divided into cell expansion and cell cultivation, and generally takes 35 days.

- *Cell recovery*. Resuscitation of cells that are cryopreserved at or below minus 130°C.

- *Cell expansion*. We thaw the cells and transfer the seed cell culture from shaker flasks to larger vessels such as bioreactors to increase the number of viable cells needed for production.

- *Cell cultivation.* We cultivate the cells to produce the target protein.

Purification

The purification stage is generally divided into three steps and takes seven to ten days.

- *Depth filtration and filtration*. The cell culture is further processed by removing cells and cell debris through depth filtration and filtration. Depth filtration primarily removes cells from the culture solution, and filtration primarily removes smaller cell debris and controls bioburden during the harvest.

- *Multi-step chromatography and viral inactivation*. Impurities are removed through multi-step chromatography. Leveraging our protein engineering expertise and platforms, our BsAb candidates are stably formulated, therefore the general chromatographic steps for our BsAb candidates are similar to sdAbs and conventional mAbs. Viruses are inactivated by altering the pH, temperature and other conditions.

- *Nanofiltration and ultrafiltration*. Viruses of all sizes are filtered and removed by passing through nanometer-sized pores on a nanofiltration membrane. For products requiring relatively highly-concentrated antibody solutions, ultrafiltration is used after nanofiltration to reach the final desired product concentration. Most of our product candidates require ultrafiltration.

- *Bulk*. Drug substances are generated for final product manufacturing.

Drug Product Manufacturing

The drug product manufacturing stage is generally divided into two steps.

- *Formulation*. Drugs are produced using predetermined formulations. Some formulations may require adding buffer solutions.

- *Fill-finish*. The final product will undergo aseptic filtration, filling, stoppering, capping, inspection, labelling and packaging.

CMOs

During the Track Record Period, we outsourced certain manufacturing activities of our drug candidates to select industry-recognized Independent Third Party CMOs in China and the United States. Such outsourcing occurs when it is more efficient than manufacturing in-house and when we seek to reduce regulatory compliance costs for clinical trials. We select CMOs by considering a number of factors, such as manufacturing capacity and qualifications, geographic proximity and track record. To monitor and evaluate the services of our CMOs, we conduct on-site audits every year to ensure full compliance of our CMOs with the relevant regulatory requirements. We review the manufacturing records for each batch of products manufactured by the CMOs.

We enter into statement of work (SOW) agreements with certain CMOs, which set out the terms with respect to placing orders, payment schedule, regulatory compliance requirements, delivery acceptance, remedy for non-conforming products, confidentiality, intellectual property and termination. Under the SOW agreements, we submit purchase orders which specify the deliverables types, unit price, volume and requested manufacturing/delivery date of each batch. We are entitled to remedies for products that fail to conform to specifications and cGMP.

QUALITY MANAGEMENT

We believe that quality control and quality assurance are crucial, and we endeavor to ensure the quality of our operations through a comprehensive quality management system. Our quality control is primarily focused on the quality of raw materials, manufacturing process and finished products.

Our quality management team has established a set of comprehensive quality control and quality assurance procedures to monitor that our manufacturing process comply with relevant regulatory requirements and our internal quality requirements. We select qualified raw material suppliers, and recruit manufacturing and quality management personnel based on a strict set of criteria. We regularly validate our facilities and equipment to ensure that our processes, methods, programs and equipment work properly. We set a series of pre-defined specifications on in-process control and release tests, and review manufacturing-related documents, including batch records and quality control test results, to ensure specifications are met. For critical process parameters and critical quality attributes, we closely monitor the results and perform two rounds of inspections by different personnel. We also monitor the manufacturing environment, especially special requirements such as microbial and specified temperature and humidity. In addition, we focus on designing, constructing and operating manufacturing facilities to meet applicable regulatory requirements and rigorous GMP standards. See "Manufacturing—Manufacturing Facilities." To comply with the established and latest GMP standards in our targeted markets, we pay close attention to the latest updates of cGMPs in China and the U.S. and update our internal procedures accordingly if necessary.

Our quality management team comprised 40 members as of the Latest Practicable Date and is led by Mr. YANG Shaowei, who has over 20 years of quality management experience in global and PRC pharmaceutical companies. Our quality management team is divided into four teams, namely, quality assurance, quality control, quality compliance and quality validation. Our quality assurance team is responsible for quality supervision during the

manufacturing process, including ensuring that the raw materials, work in progress and final products meet quality standards and requirements, maintaining and reviewing manufacturing records, investigating deviations from quality standards and implementing remedial and preventative measures. Our quality control team is responsible for leading control and testing activities for all materials and products. Our quality compliance team is primarily responsible for ensuring that our quality management system complies with applicable laws and regulations, keeping abreast of changes in quality and compliance matters and reviewing documents relating to manufacturing. Our quality compliance team also evaluates and conducts regular audits on the suppliers of raw materials and packaging materials. Our quality validation team is primarily responsible for ensuring that our calibration and validation procedures are implemented and meet GMP requirements and comply with applicable laws and regulations.

RAW MATERIALS

During the Track Record Period, we primarily procured cell culture media, chromatography resins, raw materials, excipients, packaging materials, nanofiltration and ultrafiltration membranes, bioreactor and single-use bioprocess bags and other ancillary materials used for our research and development activities. A majority of our raw materials are widely available, and we are able to purchase them from numerous suppliers. We have established relationships with preferred suppliers of raw materials for our manufacturing activities who we believe have sufficient capacity to meet our demands. We typically order raw materials on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. We generally have credit periods of 30 to 60 days.

SUPPLIERS

During the Track Record Period, our major suppliers primarily consisted of machinery and equipment suppliers and construction service providers for our new facilities, as well as raw materials suppliers and third-party service providers for our clinical trials and pre-clinical studies. We have maintained stable business relationships with our major suppliers for approximately two to three years. For the procurement of machinery and equipment and construction services related to our new facilities, we generally settle payments pursuant to a payment schedule. For raw material procurement, see "—Raw Materials." For CROs, see "—Research and Development—CROs."

For the years ended December 31, 2017 and 2018 and for the six months ended June 30, 2019, purchases from our five largest suppliers amounted to RMB15.3 million, RMB27.5 million and RMB22.5 million, respectively, accounting for 41.7%, 45.6% and 43.5%, respectively, of our total purchase amounts. Purchases from our largest supplier amounted to RMB5.1 million, RMB8.2 million and RMB7.4 million, respectively, for the same periods, accounting for 14.0%, 13.6% and 14.3%, respectively, of our total purchase amounts. During the Track Record Period, none of our Directors, their associates or any Shareholder who, to the knowledge of our Directors, owned more than 5% of our issued share capital, had any interest in any of our five largest suppliers.

INVENTORY MANAGEMENT

Our inventory consists of raw materials. We generally maintain an inventory level for raw materials to support one month of production needs. We have established an inventory management system that monitors each stage of the warehousing process. We have a warehouse at our manufacturing facility. Warehouse personnel are responsible for the inspection, storage and distribution of raw materials. Raw materials are separately stored in different areas of the warehouse according to their storage condition requirement, properties, usage and batch number.

INTELLECTUAL PROPERTY

We recognize the importance of intellectual property rights to our business and are committed to their development and protection. Currently, the PRC and the United States are our major target markets. As of the Latest Practicable Date, we owned one patent covering KN026 in China, co-owned one patent with 3DMed covering KN035 in Australia, and co-owned five patents with Suzhou Alphamab covering our CRIB and CRAM platforms, two of which are granted in China and one in the United States. As of the same date, we owned or co-owned 23 patent applications worldwide relating to our drug candidates and technology platforms. Of these 23 patent applications, there were four patent applications in China, three patent applications in the United States and two were PCT applications that are expected to enter into national phases in China and the United States that we consider to be material to our business. In addition, a number of patent applications were in the process of being transferred to us from Suzhou Alphamab as of the Latest Practicable Date. We also obtained exclusive licenses for two PRC patent applications and two PCT applications from Suzhou Alphamab for the development and commercialization of certain of our drug candidates. See "Connected Transactions—Exempt Continuing Connected Transaction—Patent Licensing Arrangements."

We own, co-own or have licenses to patents and/or patent applications covering KN046, KN026 and KN035 and our CRIB and CRAM platforms. KN019 is currently covered by two patents granted in China held by a third party, which are currently expected to expire in 2021. We plan to commercialize KN019, if approved, after these patents expire. For related risks, see "Risk Factors—Risks Relating to Our Intellectual Property Rights—Intellectual property and other laws and regulations are subject to change, which could diminish the value of our intellectual property and impair the intellectual property protection of our drug candidates."

The following table summarizes the details of the material patents and patent applications related to our pipeline candidates and technology platforms.

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date
KN046	PCT/CN2019/089980	Dimer and use thereof	Jiangsu Alphamab	Covering the molecule of KN046; preparation method; and usage in the treatment of cancer	PCT	Pending	Ownership	June 4, 2019	N/A[4]	N/A[2]
	PCT/CN2019/086821	Dimer and use thereof	Jiangsu Alphamab	Covering the molecule of KN046; preparation method; and usage in the treatment of cancer	PCT	Pending	Ownership	May 14, 2019	N/A[4]	N/A[2]

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date
KN026	CN2015100080458	具有共同輕鏈的雙特異性抗體或抗體混合物 (Bispecific antibody or antibody mixture having common light chains)	Jiangsu Alphamab	Covering the molecule of KN026; preparation method; and usage in the treatment of HER2 High tumor	China	Granted	Ownership	January 8, 2015	October 15, 2019	January 2035
	CN2016800051674	具有共同輕鏈的雙特異性抗體或抗體混合物 (Bispecific antibody or antibody mixture having common light chains)	Jiangsu Alphamab	Covering the molecule of KN026; preparation method; and usage in the treatment of HER2 High tumor	China	Substantive examination	Ownership	January 8, 2016	N/A[4]	N/A[2]
	US15/541921	Bispecific antibody or antibody mixture with common light chains	Jiangsu Alphamab	Covering the molecule of KN026; preparation method; and usage in the treatment of HER2 High tumor	United States	Substantive examination	Ownership	January 8, 2016	N/A[4]	N/A

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date
KN035	CN201680031072X	針對程序性死亡配體(PD-L1)的單域抗體及其衍生蛋白(Single domain antibody and derivative proteins thereof against programmed death ligand (PD-L1))	Jiangsu Alphamab; 3DMed	Covering the molecule of KN035 and usage in the treatment of cancer	China	Substantive examination	Co-ownership with 3DMed and only for oncology treatment area	August 1, 2016	N/A[4]	N/A[2]
	US15/748438	Single domain antibody and derivative proteins thereof against programmed death ligand (PD-L1)	Jiangsu Alphamab; 3DMed	Covering the molecule of KN035 and usage in the treatment of cancer	United States	Publication	Co-ownership with 3DMed and only for oncology treatment area	August 1, 2016	N/A[4]	N/A[2]

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date
CRIB	CN2011104591007	基於電荷網絡的異二聚體FC改造方法及異二聚體蛋白的製備方法 (heterodimeric FC modification method based on charge network and preparation method of heterodimeric proteins)	Jiangsu Alphamab; Suzhou Alphamab	Covering a type of modified bispecific antibodies; methods of making such antibodies; with coverage of KN026's Fc	China	Granted	Co-ownership with Suzhou Alphamab; exclusive rights in oncology treatment area	December 31, 2011	February 2015	December 2031
	CN2015109389950	基於CH3結構域的異二聚體分子、其製備方法及用途 (Heterodimer molecule based on CH3 domain, and preparation method therefor and use thereof)	Suzhou Alphamab; Jiangsu Alphamab	Covering a type of modified bispecific antibodies; methods of making such antibodies	China	Substantive examination	Co-ownership with Suzhou Alphamab; exclusive rights in oncology treatment area	December 16, 2015	N/A[4]	N/A[2]

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date
	CN2016800732863	基於CH3結構域的異二聚體分子、其製備方法及用途 (Heterodimer molecule based on CH3 domain, and preparation method therefor and use thereof)	Suzhou Alphamab; Jiangsu Alphamab	Covering a type of modified bispecific antibodies; methods of making such antibodies; with coverage of KN026's Fc	China	Substantive examination	Co-ownership with Suzhou Alphamab; exclusive rights in oncology treatment area	December 16, 2016	N/A[4]	N/A[2]
	US16/062405	Heterodimer molecule based on CH3 domain, and preparation method therefor and use thereof	Suzhou Alphamab; Jiangsu Alphamab	Covering a type of modified bispecific antibodies; methods of making such antibodies; with coverage of KN026's Fc	United States	Pending substantive examination	Co-ownership with Suzhou Alphamab; exclusive rights in oncology treatment area	December 16, 2016	N/A[4]	N/A[2]

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date[2]
CRAM	CN2013103137637	利用電荷排斥作用製備同二聚體蛋白混合物的方法 (Method for preparing homodimer protein mixture by using charge repulsion effect)	Suzhou Alphamab; Jiangsu Alphamab	Covering the method for preparing homodimer protein within a single cell line	China	Granted	Co-ownership with Suzhou Alphamab; exclusive rights in oncology treatment area	July 25, 2013	March 2015	July 2033
	US14/416817	Method for preparing homodimer protein mixture by using charge repulsion effect	Suzhou Alphamab; Jiangsu Alphamab	Covering the method for preparing homodimer protein within a single cell line	United States	Granted	Co-ownership with Suzhou Alphamab; exclusive rights in oncology treatment area	July 25, 2013	July 2017	January 2034

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date
KN035	PCT/CN2016/092679	針對程序性死亡配體 (PD-L1) 的單域抗體及其衍生蛋白 (Single domain antibody and derivative proteins thereof against programmed death ligand (PD-L1))	Suzhou Alphamab	Direct to the anti-PD-L1 VHH sequence as well as CDRs; usage in the treatment of cancer, infectious diseases and chronic inflammatory diseases; with coverage of KN046's anti-PD-L1 domain and part of KN035	PCT	Publication	Exclusive license to develop and commercialize in oncology treatment area	August 1, 2016	N/A[4]	N/A[2]
	CN2016800310151	針對程序性死亡配體(PD-L1)的單域抗體及其衍生蛋白 (Single domain antibody and derivative proteins thereof against programmed death ligand (PD-L1))	Suzhou Alphamab	Direct to the anti-PD-L1 VHH sequence as well as CDRs; usage in the treatment of cancer, infectious diseases and chronic inflammatory diseases; with coverage of KN046's anti-PD-L1 domain and part of KN035	China	Substantive examination	Exclusive license to develop and commercialize in oncology treatment area	August 1, 2016	N/A[4]	N/A[2]

Product/Platform	Patent Number	Patent Name[1]	Applicant/Owner	Scope of patent protection	Jurisdiction	Patent status	Rights of Alphamab Oncology	Patent application date	Grant date	Expiration date
KN046	CN2016103325907	針對CTLA4的單域抗體及其衍生蛋白(Single domain antibody and derivative proteins thereof against CTLA4)	Suzhou Alphamab; Zhang Xitian; Zhang Xin[3]	Direct to a group of anti-CTLA4 VHH sequences as well as CDRs; usage in the treatment of cancer, infectious diseases; with coverage of any anti-CTLA-4 VHH sequence or CDR in the directed group used by any monospecific antibody, BsAb or fusion protein, including KN046	China	In the phase of substantive examination and waiting to be assigned to an examiner	Exclusive license to develop and commercialize in oncology treatment area	May 19, 2016	N/A[4]	N/A[2]
	PCT/CN2017/085038	針對CTLA4的單域抗體及其衍生蛋白(Single domain antibody and derivative proteins thereof against CTLA4)	Suzhou Alphamab; Zhang Xitian; Zhang Xin[3]	Direct to a group of anti-CTLA4 VHH sequences as well as CDRs, usage in the treatment of cancer, infectious diseases; with coverage of any anti-CTLA-4 VHH sequence or CDR in the directed group used by any monospecific antibody, BsAb or fusion protein, including KN046	PCT	National phase applications have been submitted in China and the US, among others	Exclusive license to develop and commercialize in oncology treatment area; worldwide	May 19, 2017	N/A[4]	N/A[2]

Abbreviation: N/A = not applicable

(1) Invented by Dr. Xu and individual(s) that contributed to the invention due to his/her services under employment. No inventors have ownership to the relevant patent rights.

(2) Subject to these patents being granted, the patent expiration date will be 20 years after the patent application date.

(3) Ms. Zhang Xin is the daughter of Mr. ZHANG Xitian. From October 2015 to March 2018, Suzhou Alphamab entered into a series of agreements with Mr. ZHANG Xitian, Ms. Zhang Xin and PRC companies controlled by Ms. Zhang Xin, under which, among others, Suzhou Alphamab, Mr. ZHANG Xitian and Ms. Zhang Xin co-filed the patent application and agreed that (i) Mr. ZHANG Xitian and Ms. Zhang Xin only have exclusive rights to use the patent application and any patent granted under the patent application, on their own or in the form of out-licensing, for the purpose of research, development, production and commercialization of a single anti-CTLA-4 monospecific antibody, which applies a specific sequence in the anti-CTLA-4 VHH sequence group directed by this patent application. See "—Scope of patent protection" set forth above; and (ii) other than the aforementioned particular anti-CTLA-4 monospecific antibody, Suzhou Alphamab has exclusive rights to use the patent application and any patent granted under the patent application, on its own or in the form of out-licensing, for the purpose of research, development, production and commercialization of any BsAb, fusion protein and any other monospecific antibody. As a result, Suzhou Alphamab and the two individuals have contractually divided their patent rights to the patent application for the purpose of development and commercialization of non-overlapping products. According to CIC, such practice is not uncommon in the pharmaceutical industry. As the patent rights of Suzhou Alphamab and the two individuals have been clearly delineated under relevant agreements, and we developed KN046 only with patent rights to the patent application exclusively licensed by Suzhou Alphamab to Jiangsu Alphamab in oncology treatment area, our PRC Legal Adviser is of the view that neither Mr. ZHANG Xitian nor Ms. Zhang Xin has any patent rights or interests in the patent application in relation to KN046 with respect to its research, development, application, manufacturing or commercialization.

(4) As at the Latest Practicable Date, these patents had not yet been granted.

The term of individual patents may vary based on the countries in which they are obtained. In most countries in which we have filed patent applications, including China and the United States, the term of a granted patent is generally 20 years from the filing date of the earliest non-provisional patent application on which the patent is based in the applicable country. In the United States, a patent's term may be lengthened in some cases by a patent term adjustment, which extends the term of a patent to account for administrative delays by the USPTO, in excess of a patent applicant's own delays during the prosecution process, or may be shortened if a patent is terminally disclaimed over a commonly-owned patent having an earlier expiration date.

In addition, in the United States, we may apply for a patent term extension of up to five years as compensation for the patent term lost during clinical trials and the FDA regulatory review process under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The exact duration of the extension depends on the time we spend in clinical studies, as well as getting a BLA approval from the FDA. However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended per drug and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. In certain other foreign jurisdictions, similar extensions as compensation for regulatory delays are also available.

We conduct our business under the brand name of "Alphamab Oncology" ("康寧傑瑞"). As of the Latest Practicable Date, we owned one trademark in Hong Kong and seven trademarks in China. We have entered into an agreement with Suzhou Alphamab, pursuant to which Suzhou Alphamab will become a co-owner of two of our PRC trademarks. We also had three domain names. For more information, see "Appendix V—Statutory and General Information—B. Further Information about Our Business—2. Intellectual Property Rights" to this Prospectus.

We rely on a combination of patents, trademarks and trade secrets as well as employee and third-party confidentiality agreements to safeguard our intellectual property. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except under specific circumstances. Further, as a matter of our risk management policy, all of our key scientific and technical employees have entered into agreements that generally require disclosure and assignment to us of ideas, developments, discoveries and inventions made by them which are relating to their employment with us.

As of the Latest Practicable Date, we were not involved in any proceedings in respect of, and we had not received notice of any claims of infringement of, any intellectual property rights that may be threatened or pending, in which we may be a claimant or a respondent.

EMPLOYEES

As of the Latest Practicable Date, we had a total of 220 employees. The table below sets forth our employees by function as of the Latest Practicable Date.

	Number of employees
Management	10
Research and development	68
Audit and internal control	4
Manufacturing	64
Procurement warehouse	11
Quality management	40
Operations	23
Total	220

We recruit our employees through recruitment websites, recruiters, internal referral and job fairs. We conduct new employee training, as well as professional and compliance training programs for employees of the commercialization team.

We enter into employment contracts with our employees to cover matters such as wages, benefits and grounds for termination. The remuneration package of our employees includes salary and bonus, which are generally determined by their qualifications, industry experience, position and performance. We make contributions to social insurance and housing provident funds as required by the PRC laws and regulations.

As of the Latest Practicable Date, we had not established a labor union. During the Track Record Period and as of the Latest Practicable Date, we did not experience any material labor disputes or strikes that may have a material and adverse effect on our business, financial condition or results of operations.

INSURANCE

We maintain insurance policies that are required under PRC laws and regulations as well as based on our assessment of our operational needs and industry practice. We maintain insurance for our new facilities. In line with industry practice in the PRC, we have elected not to maintain certain types of insurances, such as business interruption insurance or key man insurance. Our Directors consider that our existing insurance coverage is sufficient for our present operations and in line with the industry practice in the PRC.

LICENSES AND PERMITS

We are subject to regular inspections, examinations and audits, and are required to maintain or renew the necessary permits, licenses and certifications for our business. Our PRC Legal Adviser has advised us that, as of the Latest Practicable Date, we had obtained all requisite licenses, approvals and permits from the relevant government authorities that are material for our business operations in the PRC.

PROPERTIES

Owned Properties

Our headquarters are located in Suzhou, Jiangsu province. As of the Latest Practicable Date, we owned land use rights to one parcel of land in the PRC, with an area of 50,001.45 square meters. We are constructing buildings on such land that will become our manufacturing and research and development facilities. Phase I of our new facilities will have a planned GFA of 53,867 square meters and is expected to be completed in late 2019.

The Property Valuation Report produced by JLL, an independent property valuer, set out in Appendix III to this Prospectus sets out details of our owned land and construction-in-progress thereon as of October 31, 2019. JLL valued our owned property interests at an amount of approximately RMB230.6 million as of October 31, 2019. The parcel of land was pledged as collateral for bank borrowing. See "Financial Information—Indebtedness" for details. As advised by our PRC Legal Adviser, subject to such pledge, we are entitled to occupy and use this parcel of land within the scope and term of use specified in the real estate ownership certificate.

Leased Properties

As of the Latest Practicable Date, we leased five properties with an aggregate GFA of approximately 2,899.16 square meters, one of which is leased from Suzhou Alphamab. The following table sets forth the details of our leased properties as of the Latest Practicable Date.

Location	Use	GFA	Lease term
		(square meter)	
Room 721, 800 Shangcheng Road, Pudong New Area, Shanghai, China	Office premises	55.5	June 26, 2018 to June 25, 2020

Location	Use	GFA	Lease term
		(square meter)	
Room 722, 800 Shangcheng Road, Pudong New Area, Shanghai, China	Office premises	144.53	June 26, 2018 to June 25, 2020
Room 618, 800 Shangcheng Road, Pudong New Area, Shanghai, China	Office premises	216.13	February 14, 2019 to February 13, 2021
A22, Room 200, Basement 1, Building 50, Yard 63, West Dawang Road, Chaoyang District, Beijing, China	Office premises	248	January 28, 2019 to February 27, 2021
4th floor and 5th floor of Building C23, SIP BioBay, No. 218 Xinghu Street, Suzhou, Jiangsu Province, China	Manufacturing and research and development	2,235	June 1, 2019 to December 31, 2021

We have required all of our lessors to provide the necessary documentation and valid title certificates before we entered into lease agreements with them and we will not enter into lease agreements for properties with title defects. As of the Latest Practicable Date, all five of these lease agreements had not been registered with relevant authorities. Our PRC Legal Adviser is of the view that the non-registration of lease agreements will not affect the validity of the lease agreements and our use of such properties, but the relevant local housing administrative authorities can require us to complete registrations within a specified timeframe and we may be subject to a fine of between RMB1,000 and RMB10,000 for any delay in making registration for each of these leasing properties.

ENVIRONMENTAL PROTECTION, OCCUPATIONAL HEALTH AND SAFETY

We are subject to environmental protection and occupational health and safety laws and regulations in China. However, as we did not commence manufacturing during the Track Record Period, we did not incur material environmental protection expenses during such period. During the Track Record Period and as of the Latest Practicable Date, we complied with the relevant environmental and occupational health and safety laws and regulations in China and we did not have any incidents or complaints, which had a material and adverse effect on our business, financial condition or results of operations during the same period.

We strive to provide a safe working environment for our employees. We have implemented work safety guidelines setting out safety practices, accident prevention and accident reporting. Our employees responsible for manufacturing and quality control and assurance are required to hold relevant qualifications, as well as wear the proper safety gear when working.

AWARDS AND RECOGNITION

The table below sets forth a summary of the major awards and recognition we received during the Track Record Period.

Award/Recognition	Award date	Awarding authority
Best Biomedical Investment Case Award in 2019 (2019年度生物醫藥最佳投資案例獎)	April 2019	Haoyue Capital (浩悦資本)
Developing Unicorn Enterprise in Suzhou in 2018 (2018年度蘇州市獨角獸培育企業)	October 18, 2018	Office of People's Government of Suzhou City (蘇州市人民政府辦公室)
Future Medical Company Top 100 in 2018–China Pharmaceutical List Top 100 (2018未來醫療100強-中國醫藥榜TOP100)	December 2018	VCBeat Research (蛋殼研究院)
Best Investment Value Healthcare Company (2017年度最具投資價值醫療健康企業)	2017	China Healthcare Consulting

COMPLIANCE AND LEGAL PROCEEDINGS

We may be involved in legal proceedings in the ordinary course of business from time to time. During the Track Record Period and as of the Latest Practicable Date, neither we nor our Directors were involved in any litigation, arbitration or administrative proceedings, which could have a material adverse impact on our business, financial condition or results of operations. As of the Latest Practicable Date, we were not aware of any pending or threatened litigation, arbitration or administrative proceedings against us or our Directors, which may have a material and adverse impact on our business, financial condition or results of operations.

As advised by our PRC Legal Adviser, during the Track Record Period and as of the Latest Practicable Date, we had complied with the relevant PRC laws and regulations in all material respects.