OVERVIEW

We are an integrated and innovative biopharmaceutical company committed to the R&D, manufacturing and commercialization of novel drugs to address medical needs in China and globally. Empowered by our integrated drug development capabilities and a well-established management system that covers all key business functionalities, we are dedicated to the in-house development of differentiated treatments to improve the existing standard of care. Notably, we are one of the first movers and a leading developer of antibody drug conjugates (ADCs), with over a decade of accumulated experience in ADC development. We are one of the first biopharmaceutical companies in China, and one of the few globally, to establish an integrated ADC platform, *OptiDC*.

We take a systematic, indication-oriented approach to target the world's prevalent or hard-to-treat cancers, and other diseases and conditions affecting a large and underserved population. Over the years, we have developed integrated capabilities encompassing all key drug development functionalities, including R&D, manufacturing, quality control and commercialization, which empower us to rapidly and strategically advance a differentiated and clinically valuable pipeline of 33 assets, including 14 in clinical stage as of the Latest Practicable Date. Supported by three in-house developed technology platforms with proprietary know-how in ADCs, biologics (monoclonal antibodies (mAbs) and bispecific antibodies (bsAbs)) and small molecule drugs and validated by our clinical-stage drug candidates, our pipeline is diverse and synergistic in drug modalities, mechanisms, and indication coverage. Our drug development capabilities are further bolstered by current good manufacturing practice (cGMP)-compliant, end-to-end manufacturing capabilities and a comprehensive quality control system. Furthermore, we are well-positioned to expand our commercialization infrastructure and market access, leveraging our Controlling Shareholder Kelun Pharmaceutical's decades-long experience, industry connections and extensive network.

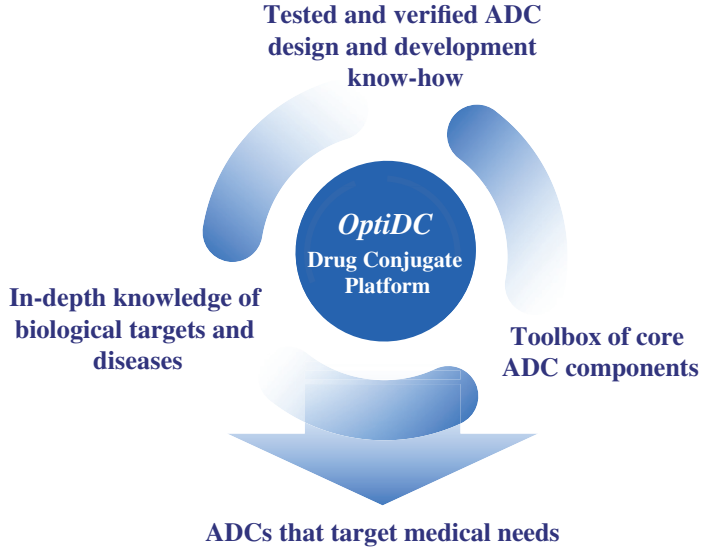
The clinical value of our pipeline and our drug development capabilities are recognized by the strategic partnerships we have forged worldwide to unlock the global market potential of key assets. To date, we have entered into nine out-license agreements, including three license and collaboration agreements with Merck Sharp & Dohme LLC (together with its affiliates, "MSD") to develop up to nine ADC assets for cancer treatment with upfront and milestone payments totaling up to US$11.8 billion. According to Frost & Sullivan, we are the first China-based company to license internally discovered and developed ADC candidates to a top-ten biopharmaceutical MNC. Our collaboration with MSD to develop up to seven preclinical ADC assets is the largest biopharmaceutical out-license deal to date secured by a China-based company, according to Frost & Sullivan, and the world's largest biopharmaceutical partnership in terms of deal value in 2022, according to Nature Reviews Drug Discovery. We have also entered into collaboration and license agreements with Ellipses for A400, and with Harbour BioMed for A167 and SKB378. Our strategic partnerships are not only testaments to our R&D and business development capabilities, but also key drivers of our continued innovation, global influence and long-term growth.

Going forward, we strive to advance our pipeline towards commercialization and enhance our integrated drug development capabilities. We will continue to lead the R&D and clinical activities of our drug candidates, including, for assets out-licensed to our strategic partners, in the regions where we retain the rights to their development and commercialization. In addition, we are dedicated to optimizing our R&D platforms and developing novel technologies to support the R&D of innovative drugs. We will also continue to expand our cGMP manufacturing and quality control facilities, and enhance our in-house commercialization functionalities, to support the future launch of our pipeline assets and our goal to become a leading global biopharmaceutical company.

Our Technology Platforms

We have established three core platforms specializing in ADC, biologics and small molecule technologies that serve as the foundation of our discovery and development of innovative medicines for medical needs in selected disease areas, such as oncology, autoimmune diseases and metabolic diseases. These platforms cover the entire R&D process for different drug modalities and are integrated to allow cross-functional synergies at crucial stages of drug development.

- ***ADC Platform***. We are one of the first movers and a leading developer of ADCs, with over a decade of accumulated experience in ADC development. According to Frost & Sullivan, we are one of the first biopharmaceutical companies in China, and one of the few globally, to establish an integrated ADC development platform, which supports our systematic development of ADCs across their entire lifecycle. Our ADC platform, *OptiDC*, is supported by three capability pillars – in-depth knowledge of biological targets and diseases, tested and verified ADC design and development know-how, and a toolbox of core ADC components. Through over a decade of development, we have developed a toolbox of core ADC components which gives us the versatility to engineer customized ADCs optimized for different biological targets to address medical needs in a broad range of indications. We have honed our expertise in ADC process development, manufacturing and quality control, which we believe is crucial in bringing our ADCs from bench to bedside. Notably, our ADC platform is tested and verified through preclinical studies and clinical trials with over 1,160 patients as of the Latest Practicable Date.



Our platform has been tested through extensive studies and trials, including validation from over ten clinical or preclinical ADC candidates. Our ADC design strategies are exemplified by *Kthiol*, our proprietary drug-linker strategy implemented in SKB264. An optimized balance between safety and efficacy is achieved in this strategy by incorporating a novel irreversible antibody conjugating technology, a pH-sensitive toxin release mechanism, and a moderately potent toxin homogeneously loaded with DAR 7.4. Our continued advancement in ADC research and development forms a feedback loop that strengthens our platform, and enables our consistent and rapid delivery of highly competitive ADC candidates.

- ***Biologics Platform***. Our extensive biologics technology platform, while complementing our ADC platform, serves as the foundation of our immunotherapy and targeted therapy franchises. This platform is focused on mAbs and bsAbs and possesses end-to-end antibody development capabilities ranging from antibody discovery and optimization to bioprocessing and scale-up manufacturing. As of the Latest Practicable Date, we had six clinical assets and various preclinical assets developed under our biologics platform. Our clinical assets include two mAbs at pivotal phase 3 or NDA registration-stage, A167 (PD-L1) and A140 (EGFR), as well as SKB337 (PD-L1/CTLA4), A289 (LAG3), SKB378 (TSLP) and SKB336 (FXI/FXIa). Our preclinical assets are mainly antibodies with novel targets and differentiated mechanisms of action that potentially enable broad clinical applications and reduced drug resistance.

- ***Small Molecule Platform***. Our small molecule platform is driven by the integration of medicinal chemistry and computer-aided drug design (CADD) technologies, such as molecular docking, pharmacophore modeling, virtual screening and absorption, distribution, metabolism, elimination and toxicity (ADMET) prediction. These capabilities allow us to focus on compound optimization in early-stage research, which help rationalize and accelerate our preclinical drug discovery. Leveraging this platform, we have built an innovative pipeline of four clinical-stage small molecule drug candidates, including A400 (selective RET inhibitor), A223 (JAK1/2 inhibitor), A296 (STING agonist) and A277 (KOR agonist), and various preclinical assets. We are also exploring state-of-the-art technologies such as proteolysis targeting chimera (PROTAC) to navigate challenging protein targets, with one small-molecule PROTAC candidate currently at IND-enabling stage.

Our Pipeline

Our pipeline targets the world's prevalent or hard-to-treat cancers, such as breast cancer (BC), non-small cell lung cancer (NSCLC), gastrointestinal (GI) cancers (including gastric cancer (GC) and colorectal cancer (CRC)), as well as non-oncology diseases and conditions affecting a large and underserved population. As of the Latest Practicable Date, we had established a pipeline of 14 clinical-stage drug candidates, including five in pivotal trial- or NDA registration-stage. We have also assembled a diverse portfolio of preclinical assets, including four in IND-enabling stage, to further enrich our expanding pipeline targeting medical needs. The pipeline chart below summarizes the development status of our clinical-stage drug candidates and selected preclinical assets.

Abbreviations: TNBC: triple-negative breast cancer; BC: breast cancer; NSCLC: non-small-cell lung cancer; NPC: nasopharyngeal cancer; GC: gastric cancer; OC: ovarian cancer; SCLC: small-cell lung cancer; UC: urothelial cancer; HNSCC: head and neck squamous cell carcinoma; EC: endometrial cancer; CRPC: castration-resistant prostate cancer; CRC: colorectal cancer; MTC: medullary thyroid cancer; CKD-aP: chronic kidney disease-associated pruritus

Notes:

1. Including immunotherapy and targeted therapies; 2. No phase II clinical trial is required for biosimilar drug candidates in China; 3. CDE consultation completed; 4. We completed a phase 1a study and are conducting a phase 1b study. Based on the NMPA's approval, we also commenced a pivotal phase 2 clinical trial. Upon meeting the primary endpoint in this trial, we filed NDA for conditional approval, which is under priority review. Although we completed the study per protocol, the trial is ongoing as certain patients responsive to the drug continue with treatment. Pending consultation with the CDE, we plan to commence a confirmatory phase 3 trial in 2H 2023; 5. CDE consultation ongoing; 6. A phase 1a and pivotal phase 2 clinical trial was completed. We commenced a confirmatory phase 3 trial upon consultation with the CDE; 7. Phase 1a/1b trial.

Our oncology franchise features diversified treatment modalities and targets different mechanisms to comprehensively treat prevalent or hard-to-treat cancers in China and worldwide, anchored by the following assets:

- ***SKB264 (sacituzumab tirumotecan)***, one of our Core Products, is a novel TROP2 ADC targeting advanced solid tumors. Drugs that successfully target TROP2 have vast market potential as TROP2 is frequently overexpressed across a broad spectrum of cancers, especially in highly prevalent or hard-to-treat cancers such as BC, NSCLC, GC and OC. The global TROP2 ADC market is expected to increase from US$0.7 billion in 2022 to US$25.9 billion by 2030, representing a CAGR of 57.6%, while the TROP2 ADC market in China, following the NMPA approval of the first TROP2 ADC in June 2022, is projected to grow from RMB0.2 billion in 2023 to RMB23.6 billion by 2030 at a CAGR of 103.0%.

  Positioned to be the first domestically developed TROP2 ADC in China, SKB264 utilizes a differentiated drug design to improve ADC stability and maintain ADC bioactivity, thus enhancing its targeting ability and reducing its off-target and on-target off-tumor toxicity, potentially leading to a broader therapeutic window. Preliminary clinical data from SKB264's global phase 1/2 trial showed that SKB264 demonstrated encouraging ORRs across multiple types of heavily pretreated advanced solid tumors, highlighted by an ORR of 43.6%, 42.9% and 43.6% in heavily pre-treated TNBC, HR+/HER2- BC and NSCLC patients, respectively. SKB264 also demonstrated a potentially favorable safety profile. Based on non-head-to-head cross-trial comparisons, SKB264 demonstrated lower incidences of decreased neutrophil count (54% vs 78% for all grades, 26% vs 49% for ≥ grade 3) and diarrhea (4% vs 59% for all grades, 0% vs 11% for ≥ grade 3) compared with Trodelvy; and no incidence of treatment-related interstitial lung disease (ILD) compared with that reported in DS-1062-treated patients (6% for all grades and 2% for ≥ grade 3). We are also exploring SKB264's early-line potential in combination therapy. Based on preliminary results from a phase 2 trial conducted in China, SKB264 in combination with A167 demonstrating a promising ORR of 85.7% as a first-line therapy in advanced TNBC patients.

  Supported by its promising proof-of-concept results, SKB264 was granted Breakthrough Therapy Designation by the NMPA for advanced TNBC in July 2022 and for EGFR-TKI failed EGFR-mutant advanced NSCLC in January 2023. In May 2022, we granted MSD exclusive development and commercialization rights for SKB264 outside Greater China. See "– Our License and Collaboration Arrangements – License and Collaboration Agreement with MSD for SKB264" for details.

  We are actively advancing a multi-strategy clinical development plan to explore SKB264's potential as a monotherapy and combination therapies to treat various advanced solid tumors, including BC, NSCLC and other major cancers. For details, see "– Our Pipeline – Oncology Franchise – ADCs – SKB264 – Clinical Development Plan."

- ***A166 (trastuzumab botidotin)***, another Core Product, is a differentiated HER2 ADC in NDA registration stage to treat advanced HER2+ solid tumors. It is positioned to target multiple cancer indications with high prevalence and medical needs, with the potential to be one of the first domestically developed ADCs for HER2-positive (HER2+) BC in China. HER2 overexpression is widely recognized as a major driver of prevalent cancers, including BC and GI cancers.

  Configured with a potent cytotoxic payload, clinically proven mAb and site-specific conjugation technology, A166 demonstrated promising efficacy in heavily pre-treated advanced HER2+ BC patients with an ORR of 73.9% at RP2D and in advanced HER2+ GC patients with an ORR of 31.3%, based on preliminary results from our ongoing phase 1 dose expansion study and ongoing phase 1b trial in China. A166 also showed a differentiated safety profile from that of Kadcyla, Enhertu and Aidixi, the only three FDA and/or NMPA-approved HER2 ADCs as of the Latest Practicable Date, with lower incidence of haematological, GI and lung toxicities in non-head-to-head, cross-trial comparisons. Although A166 demonstrated higher incidences of ocular and peripheral nerve-related toxicities, they were reversible and generally manageable. A166 has met the primary endpoints of its pivotal phase 2 trial for advanced HER2+ BC based on results from the primary analysis, which we used to submit an NDA to the NMPA in May 2023. In addition to our pivotal phase 2 trial for advanced HER2+ BC, we are exploring the therapeutic potential of A166 in multiple ongoing phase 1b clinical trials in China for other advanced HER2+ solid tumors, including GC and CRC.

- ***SKB315*** is a novel CLDN18.2 ADC targeting advanced solid tumors. As of the Latest Practicable Date, there were no CLDN18.2-targeting therapies approved globally. Due to its selective expression in prevalent and lethal cancers that have limited effective treatments such as GC and PC, CLDN18.2 has been a promising target pursued by multiple biopharmaceutical and biotech companies for in-house development and licensing deals. In June 2022, we out-licensed the global development and commercialization rights for SKB315, currently in phase 1a clinical trial, to MSD. With a differentiated payload-linker design and an in-house developed humanized CLDN18.2 antibody, SKB315 demonstrated encouraging efficacy and safety across various preclinical *in vivo* tumor models with heterogeneous CLDN18.2 expression, indicating its promising therapeutic potential.

- ***A167 (tagitanlimab)***, our PD-L1 mAb, is expected to be our first commercialized product and the backbone of our immunotherapy franchise, with an NDA submitted to the NMPA for recurrent or metastatic nasopharyngeal carcinoma (RM-NPC) in November 2021 and conditional marketing approval expected in the second half of 2023 or the first half of 2024. We are actively exploring A167's potential as an early-line treatment in combination with our ADC assets to maximize the clinical value of our oncology franchise, beginning with two ongoing phase 2 trials – a phase 2 trial of SKB264 in combination with A167 with or without chemotherapy, as an early-line treatment for advanced EGFR-wild type and EGFR-mutant NSCLC and a phase 2 trial of SKB264 with or without A167 as a first-line treatment for advanced TNBC.

- ***A140***, a pivotal phase 3 biosimilar of EGFR mAb cetuximab. A140 has potential to be the first cetuximab biosimilar in China with an anticipated NDA filing in the second half of 2023, providing increased accessibility and affordability for a widely used therapeutic targeting a key pathway in many cancers, starting with rat sarcoma virus (RAS) wild-type mCRC, recurrent and/or metastatic HNSCC (RM-HNSCC) and locally advanced HNSCC (LA-HNSCC). A140 demonstrated pharmacokinetic (PK) equivalence to cetuximab in a phase 1 trial, with clinical equivalence being evaluated in a pivotal phase 3 trial.

- ***A400***, a phase 1/2-stage second-generation selective RET inhibitor, is positioned to be the first domestically developed selective RET inhibitor for NSCLC, medullary thyroid cancer (MTC) and other solid tumors with a high prevalence of RET alterations. We have designed A400 with a novel proprietary molecular structure to potentially address selective RET inhibitor resistance while maintaining target selectivity, efficacy and safety with reduced manufacturing cost and difficulty. Based on preliminary results from its ongoing phase 1/2 trial, A400 demonstrated promising anti-tumor efficacy in patients with advanced RET+ solid tumors, highlighted by ORR of 74% and 66.7% at RP2D for 1L and 2L+ advanced RET+ NSCLC, respectively. Notably, A400 also demonstrated therapeutic potential in selective RET inhibitor-resistant patients with an ORR of 33% and DCR of 83% at RP2D, as well as a potentially favorable safety profile differentiated from approved first-generation selective RET inhibitors. In March 2021, we granted to Ellipses, a U.K.-based international drug development company, an exclusive license to develop, manufacture and commercialize A400 outside Greater China and certain Asian countries.

We will also continue to accelerate the R&D of our preclinical oncology assets. For example, we are developing over ten preclinical ADC assets with their respective targets expressed across a broad spectrum of solid tumors. See "– Our Pipeline – Oncology Franchise – ADCs – Preclinical ADC Assets." for further details. In December 2022, we entered into an exclusive license and collaboration agreement with MSD to develop up to seven preclinical ADC assets. Under this agreement, we granted MSD exclusive global licenses to research, develop, manufacture and commercialize multiple ADC assets and exclusive options to obtain additional exclusive licenses to certain other ADC assets. We retain the right to research, develop, manufacture and commercialize certain licensed and option ADCs for China, Hong Kong and Macau. For details, see "– Our License and Collaboration Arrangements – License and Collaboration Agreement with MSD for Up to Seven Preclinical ADC Assets."

Our non-oncology franchise covers a range of diseases and conditions with large patient populations and medical needs, with a primary focus on immune-mediated diseases, including rheumatoid arthritis (RA) and alopecia areata (AA). Our non-oncology franchise is headlined by A223, potentially one of the first small molecule JAK1/2 inhibitors developed domestically for multiple autoimmune diseases with large patient populations, including RA and AA, in China. A223 has demonstrated an encouraging safety profile in three completed trials and two ongoing trials, where most TEAEs were mild or moderate with no incidence of black box

warning-related safety issues commonly reported by approved JAK inhibitors. Based on preliminary clinical data from its phase 2 trial, A223 demonstrated promising anti-rheumatic efficacy in moderate-to-severe RA patients, with A223 2 mg achieving substantial and statistically significant ACR20 and ACR50 differences at week 12 compared with placebo. Notably, based on non-head-to-head comparison, the ACR20 and ACR50 differences achieved by A223 2 mg are greater than those of Olumiant 4 mg, the approved dosage of Olumiant in China, in Chinese patients with moderate-to-severe RA. These promising clinical results indicates the potential of A223 to be an effective treatment option with improved efficacy and safety for RA. Besides RA, A223 also target AA, a common autoimmune disease that affected approximately 4.0 million people in China in 2022.

In addition to A223, we are also evaluating three other clinical-stage assets (A277, SKB378 and SKB336) and various preclinical assets to target indications ranging from chronic kidney disease (CKD)-associated pruritus (CKD-aP), moderate-to-severe asthma, thromboembolic disorders, to other diseases and conditions with large patient populations and medical needs. Apart from our existing assets, we will continue to develop novel non-oncology drug candidates to address highly prevalent chronic diseases currently without effective treatments, including autoimmune and metabolic diseases.

Our Integrated Drug Development Capabilities

We have developed integrated capabilities encompassing all key drug development functionalities, including R&D, manufacturing, quality control and commercialization. Our drug development capabilities are governed by a well-established management system that covers all key business functionalities, which provides a framework for our internal teams to engage in constructive dialogue and evaluation, particularly when making critical decisions for each drug development plan. Meanwhile, we implement a dynamic global business development strategy to maximize the commercial value of our pipeline in major international markets, leveraging our experience in forging strategic partnerships worldwide.

Our in-house R&D capabilities, built on three technology platforms, give us control and visibility over our R&D process, reduces our reliance on CROs and enable us to ensure the quality and efficiency of our drug development programs. Our drug development capabilities are further bolstered by cGMP-compliant, end-to-end manufacturing capabilities that cover the entire development lifecycle of ADCs, including two 2,000 litre (L) single-use bioreactors, one 300 L ADC conjugation tank with a maximum annual production capacity of 40 batches of ADC drug substance and facilities for payload-linker synthesis, antibody formulation and ADC formulation, as well as a comprehensive quality control system. We are building up our commercialization infrastructure in anticipation of our late-stage drug candidates' commercial launch in China, leveraging our Controlling Shareholder Kelun Pharmaceutical's decades-long experience, industry connections and extensive network.

Our drug development capabilities are recognized by the breadth, depth and commercial value of the strategic partnerships we have forged worldwide, including three license and collaboration agreements with MSD to develop up to nine ADC assets for cancer treatment. These landmark transactions speak to the quality and soundness of our capabilities in every key step of our ADC development process, from drug discovery to manufacturing and quality control.

OUR COMPETITIVE STRENGTHS

Integrated ADC development platform, "*OptiDC*," with a competitive ADC drug portfolio to address medical needs globally

We are one of the first movers and a leading developer of ADCs, with over a decade of accumulated experience in ADC development. According to Frost & Sullivan, we are one of the first biopharmaceutical companies in China, and one of the few globally, to establish an integrated ADC development platform, *OptiDC*, which supports our systematic development of ADCs across their entire lifecycle. Our ADC platform is the engine for our continued innovation, and has been validated by our deep ADC drug portfolio of over ten clinical and preclinical assets.

ADCs have become one of the fastest-growing treatment modalities for cancer in recent years. Combining the target selectivity of antibodies and the cell-killing potency of cytotoxic drugs, ADCs are designed to utilize an antibody to deliver cytotoxic drugs selectively to tumor cells, potentially reducing the significant off-target toxicity associated with classic chemotherapy while using highly potent cytotoxic drugs, thereby leading to improved therapeutic window and efficacy. ADCs have presented a major scientific challenge to researchers due to the high degree of technological sophistication required to design and produce a balanced drug. Only recently have ADCs begun to gain momentum, with a total of 12 FDA-approved ADCs to date, including Enhertu (HER2-directed) and Padcev (Nectin-4-directed) in 2019 and Trodelvy (TROP2-directed) in 2020 for the treatment of solid tumors. ADCs have progressed from a late-line treatment in selected blood cancers to a promising early-line therapeutic modality for broader solid tumor indications and beyond. Globally, the ADC market is expected to grow at a 30.0% CAGR from approximately US$7.9 billion in 2022 to approximately US$64.7 billion by 2030. In China, the ADC market is expected to grow at a 72.8% CAGR from approximately RMB0.4 billion in 2022 to about RMB66.2 billion by 2030.

Through over a decade of development, we have established an integrated ADC development platform, *OptiDC*, with three capability pillars – in-depth knowledge of biological targets and diseases, tested and verified ADC design and development know-how, and a toolbox of core ADC components. Through over a decade of development, we have developed a toolbox of core ADC components, which gives us the versatility to engineer customized ADCs optimized for different biological targets to address medical needs in a broad range of indications. We have honed our expertise in ADC process development, manufacturing and quality control, which we believe is crucial in bringing our ADCs from bench to bedside. These technologies and capabilities are the backbone of our integrated ADC development platform, which is protected by over 40 patents and patent applications globally, and form our strategic moat against competition.

We have entered into three license and collaboration agreements with MSD to develop up to nine ADC assets for cancer treatment, with upfront and milestone payments totaling up to US$11.8 billion. MSD is a global health care company that delivers innovative health solutions. In recent years, MSD has continued to seek strategic business development opportunities to augment its robust internal pipeline, including through collaboration with us to strengthen its ADC portfolio. According to Frost & Sullivan, we are the first China-based company to license internally discovered and developed ADC candidates to a top-ten biopharmaceutical MNC. Notably, our collaboration with MSD to develop up to seven preclinical ADC assets is the largest biopharmaceutical out-license deal to date secured by a China-based company, according to Frost & Sullivan, and the world's largest biopharmaceutical partnership in terms of deal value in 2022, according to Nature Reviews Drug Discovery. These landmark transactions speak to the quality and soundness of our capabilities in every key step of the ADC development process, from drug discovery to manufacturing and quality control.

Equipped with deep expertise in this field, we are well positioned to further explore new frontiers of ADC technology to address medical needs. We are establishing novel ADC designs to further advance our ADC portfolio via a multi-pronged strategy, including (i) further optimizing our payload/linker technologies to solidify our ADC capabilities; (ii) developing bispecific ADCs (bsADCs) equipped with dual-targeting antibodies to deliver enhanced clinical benefits; (iii) developing other novel ADC designs such as immunostimulatory ADCs (iADCs), radionuclide drug conjugates (RDCs), dual-payload ADCs; and (iv) developing ADCs with non-cytotoxic payloads to target non-oncology diseases. Beyond cancers, we are extending our ADC focus to non-oncology drugs for treating chronic diseases that affect a large and underserved population, such as autoimmune and metabolic diseases. We believe our research has the potential to lead the next wave of innovation in ADC development.

Our ADC platform is exemplified by our pipeline, with over ten clinical and preclinical ADC assets to target some of the key mechanisms and pathways involved in cancer progression. Highlights of our ADC drug portfolio are set out below.

Clinical-stage Assets. Our clinical-stage ADC assets include SKB264, A166, and SKB315, and we currently have over ten ongoing trials being conducted in China and globally. Our ADC design strategies are exemplified by *Kthiol*, our proprietary drug-linker strategy to improve ADC stability and reduce off-target and on-target off-tumor toxicity.

- *SKB264*, one of our Core Products, is a novel TROP2 ADC targeting advanced solid tumors. Drugs that successfully target TROP2 have vast market potential as TROP2 is frequently overexpressed across a broad spectrum of cancers, especially in highly prevalent or hard-to-treat cancers such as BC, NSCLC, GC and OC. The global TROP2 ADC market is expected to increase from US$0.7 billion in 2022 to US$25.9 billion by 2030, representing a CAGR of 57.6%, while the TROP2 ADC market in China, following the NMPA approval of the first TROP2 ADC in June 2022, is projected to grow from RMB0.2 billion in 2023 to RMB23.6 billion by 2030 at a CAGR of 103.0%.

Positioned to be the first domestically developed TROP2 ADC in China, SKB264 utilizes a differentiated drug design to improve ADC stability and maintain ADC bioactivity, thus enhancing its targeting ability and reducing its off-target and on-target off-tumor toxicity, potentially leading to a broader therapeutic window. Preliminary clinical data from SKB264's global phase 1/2 trial showed that SKB264 demonstrated encouraging ORRs across multiple types of heavily pretreated advanced solid tumors, highlighted by an ORR of 43.6%, 42.9% and 43.6% in heavily pre-treated TNBC, HR+/HER2- BC and NSCLC patients, respectively. SKB264 also demonstrated a potentially favorable safety profile. Based on non-head-to-head cross-trial comparisons, SKB264 demonstrated lower incidences of decreased neutrophil count (54% vs 78% for all grades, 26% vs 49% for ≥ grade 3) and diarrhea (4% vs 59% for all grades, 0% vs 11% for ≥ grade 3) compared with Trodelvy; and no incidence of treatment-related ILD compared with that reported in DS-1062-treated patients (6% for all grades and 2% for ≥ grade 3). We are also exploring SKB264's early-line potential in combination therapy. Based on preliminary results from a phase 2 trial conducted in China, SKB264 in combination with A167 demonstrating a promising ORR of 85.7% as a first-line therapy in advanced TNBC patients.

Supported by its promising proof-of-concept results, SKB264 was granted Breakthrough Therapy Designation by the NMPA for advanced TNBC in July 2022 and for EGFR-TKI failed EGFR-mutant advanced NSCLC in January 2023. In May 2022, we granted MSD exclusive development and commercialization rights for SKB264 outside Greater China. See "– Our License and Collaboration Arrangements – License and Collaboration Agreement with MSD for SKB264" for details.

We are actively advancing a multi-strategy clinical development plan to explore SKB264's potential as a monotherapy and combination therapies to treat various advanced solid tumors, including BC, NSCLC and other major cancers. For details, see "– Our Pipeline – Oncology Franchise – ADCs – SKB264 – Clinical Development Plan."

- *A166*, another Core Product, is a differentiated HER2 ADC in NDA registration stage to treat advanced HER2+ solid tumors. It is positioned to target multiple cancer indications with high prevalence and medical needs, with the potential to be one of the first domestically developed ADCs for advanced HER2+ BC in China. HER2 overexpression is widely recognized as a major driver of prevalent cancers, including BC (15-30%) and GI cancers (GC (10-30%) and CRC (3-5%)). Although three HER2 ADCs, Kadcyla Aidixi (disitamab vedotin) and Enhertu, have been approved in China, their therapeutic efficacy is limited to a minority of HER2+ solid tumor patients, thus indicating a significant unmet need for differentiated HER2 ADCs to widen the treatment options available for patients with advanced HER2+ solid tumors. The China market of HER2 ADCs is expected to increase from RMB0.6 billion in 2022 to RMB8.4 billion by 2030, representing a CAGR of 38.2%.

Configured with a potent cytotoxic payload, clinically proven mAb and site-specific conjugation technology, A166 demonstrated promising efficacy in heavily pre-treated advanced HER2+ BC patients with an ORR of 73.9% at RP2D and in advanced HER2+ GC patients with an ORR of 31.3%, based on preliminary results from our ongoing phase 1 dose expansion study and ongoing phase 1b trial in China. A166 also showed a differentiated safety profile from that of Kadcyla, Enhertu and Aidixi, the only three NMPA and/or FDA-approved HER2 ADCs as of the Latest Practicable Date, with lower incidence of haematological, GI and lung toxicities in non-head-to-head cross-trial comparisons. Although A166 demonstrated higher incidences of ocular and peripheral nerve-related toxicities, they were reversible and generally manageable. These results suggest the potential of A166 to widen the treatment options available to advanced HER2+ solid tumor patients with different susceptibility to adverse drug reactions.

In addition to our pivotal phase 2 trial for advanced HER2+ BC, we are conducting multiple phase 1b clinical trials in China to explore the therapeutic potential of A166 for other advanced HER2+ solid tumors, including GC and CRC. For details, see "– Our Pipeline – Oncology Franchise – ADCs – A166 – Clinical Development Plan."

- *SKB315* is a novel CLDN18.2 ADC targeting advanced solid tumors. As of the Latest Practicable Date, there were no CLDN18.2-targeting therapies approved globally. Due to its selective expression in prevalent and lethal cancers that have limited effective treatment, such as GC and PC, CLDN18.2 has been a promising target pursued by multiple biopharmaceutical and biotech companies for in-house development and licensing deals. In June 2022, we out-licensed the global development and commercialization rights for SKB315, currently in phase 1a clinical trial, to MSD. With a differentiated payload-linker design and an in-house developed humanized CLDN18.2 antibody, SKB315 demonstrated encouraging efficacy and safety across various preclinical *in vivo* tumor models with heterogeneous CLDN18.2 expression, indicating its promising therapeutic potential.

Preclinical Assets. Leveraging the accumulated expertise and know-how from our clinical-stage assets, we are accelerating the R&D of over ten preclinical ADC assets, with their respective targets expressed across a broad spectrum of solid tumors. Our preclinical assets strategically cover a range of high potential targets with a demonstrated role in cancer pathogenesis, with a focus on cancers with significant patient populations and for which there are limited or no effective treatments.

Combination Therapies. In addition to developing ADCs as a single agent, we are exploring combination strategies to maximize the clinical value of our oncology franchise. SKB264 is being studied in two phase 2 basket studies to explore its potential as combination therapies, including SKB264 in combination with Keytruda for selected solid tumors, and SKB264 as combination therapies (including with Keytruda, osimertinib and chemotherapy) for advanced EGFR-wild type and EGFR-mutant NSCLC. In addition, we are conducting a phase 2 trial of SKB264 in combination with A167 with or without chemotherapy, as an early-line treatment for advanced EGFR-wild type and EGFR-mutant NSCLC and a phase 2 trial of SKB264 with or without A167 as a first-line treatment for advanced TNBC.

Comprehensive pipeline of anti-tumor drugs harnessing our multi-platform technology expertise, with strong monotherapy and combination therapy potential

We believe that cancer cannot be effectively treated with a one-size-fits-all approach. Given the complexity and heterogeneity of cancers, we believe it is crucial to equip doctors with a full arsenal of anti-tumor drugs to meet the needs with different patients with higher effectiveness. With this in mind, we have built a pipeline of six clinical-stage drug candidates and various preclinical assets, together with our ADC portfolio, to systematically treat major cancer types, such as BC, NSCLC and GI cancers, by targeting major proven mechanisms of action and targets in cancer treatment today.

Enabled by our scientific prowess and synergies across multiple platform technologies, our diversified anti-tumor drug pipeline covers both immunotherapy and targeted therapy that employs innovative mAb, bsAb and small molecule drug designs, with potential as monotherapies and combination therapies. Our powerful antibody discovery engine is equipped with both established and preeminent discovery technologies to enable high throughput discovery of quality antibodies. We have also developed antibody design and engineering technologies to produce high-affinity, humanized mAbs and bsAbs with optimized pharmacological and clinical profiles. Meanwhile, our innovative small molecule platform, supported by the integration of medicinal chemistry and CADD technologies, has been instrumental in accelerating drug discovery and advancing small molecule oncology drug candidates into clinical stage. Our multi-platform technology capability has enabled us to develop differentiated assets with efficiency and quality.

Combined with our ADC platform, we are able to harness the full potential of our platform technologies to develop optimized anti-tumor drugs and extend their application to more white space indications. We focus on developing drugs for proven or well-studied targets, which can be administered as a monotherapy or in combination with our ADCs and other oncology assets. Our pipeline comprises diverse modalities including mAb, bsAb and small molecule drugs for more flexibility in exploring combination therapies.

- ***A167*** is expected to be our first commercialized product and the backbone of our immunotherapy franchise with an NDA submitted to the NMPA for RM-NPC in November 2021 and conditional marketing approval expected in the second half of 2023 or the first half of 2024. This approval, if granted, will be conditional partially

upon our commitment to complete a phase 3 trial of A167 in combination with chemotherapy as a first-line treatment for RM-NPC, for which we completed patient enrollment as of the Latest Practicable Date. We are actively exploring A167's potential as an early-line treatment in combination with our ADC assets to maximize the clinical value of our oncology franchise, beginning with two ongoing phase 2 trials – a phase 2 trial of SKB264 in combination with A167 with or without chemotherapy, as an early-line treatment for advanced NSCLC and a phase 2 trial of SKB264 with or without A167 as a first-line treatment for advanced TNBC.

- ***A140*** has potential to be the first cetuximab biosimilar in China with an anticipated NDA filing in the second half of 2023, providing increased accessibility and affordability for a widely used therapeutic targeting a key pathway in many cancers, starting with rat sarcoma virus (RAS) wild-type mCRC. Driven by its high demand in China and NRDL inclusion, cetuximab (sold under the brand name Erbitux) posted annual sales of approximately €441 million in the Asia-Pacific region in 2022. A140 demonstrated pharmacokinetic (PK) equivalence to cetuximab in a phase 1 trial, with clinical equivalence being evaluated in a pivotal phase 3 trial.

- ***A400*** is positioned to be the first domestically developed second-generation selective RET inhibitor for NSCLC, MTC and other solid tumors with a high prevalence of RET alterations. Although two first-generation selective RET inhibitors were approved in China for RET+ solid tumors as of the Latest Practicable Date, their therapeutic benefits are limited, in part, by acquired RET drug-resistant mutations and safety issues such as hypertension and hematological toxicity, underscoring the need for novel selective RET inhibitors with improved safety and better efficacy against drug resistant mutations. The China market of selective RET inhibitors is expected to increase from RMB0.3 billion in 2022 to RMB1.8 billion in 2030, representing a CAGR of 22.9%.

  We have designed A400 with a novel proprietary molecular structure to potentially address selective RET inhibitor resistance while maintaining target selectivity, efficacy and safety with reduced manufacturing cost and difficulty. Based on preliminary clinical data from its phase 1/2 trial, A400 demonstrated promising anti-tumor efficacy in patients with advanced RET+ solid tumors, highlighted by ORR of 74% and 66.7% at RP2D for 1L and 2L+ advanced RET+ NSCLC, respectively. Notably, A400 demonstrated therapeutic potential in selective RET inhibitor-resistant patients with an ORR of 33% and DCR of 83% at RP2D, as well as a potentially favorable safety profile, with no incidence of grade 3 or above lymphopenia and thrombocytopenia and substantially lower incidence of grade 3 or above cardiovascular AEs (e.g., hypertension), hematological toxicity and electrolyte abnormalities, based on non-head-to-head cross-trial comparisons with approved first-generation selective RET inhibitors. In March 2021, we granted to Ellipses an exclusive license to develop, manufacture and commercialize A400 outside Greater China and certain Asian countries.

We are also advancing several early-stage oncology assets. SKB337 is a differentiated PD-L1/CTLA-4 bsAb in phase 1 stage, with a potentially better safety and efficacy profile than monospecific PD-L1 and CTLA4 mAbs demonstrated in preclinical studies. A289 is a phase 1-stage mAb targeting LAG3, a new-generation immune checkpoint receptor, and has demonstrated its potential to synergize with PD-(L)1 mAbs and chemotherapy to promote anti-tumor response. A296, a novel second-generation small molecule STING agonist with a differentiating molecular design, has the potential to invigorate anti-tumor immunity in "cold" tumors that are unresponsive to existing immune checkpoint inhibitors and is positioned as a combination therapy to be used with our other immunotherapy assets. Meanwhile, we are exploring combination therapies between our other immunotherapy drugs, as well as with our ADC portfolio, to expand their clinical application in broad cancer types.

Well-selected non-oncology pipeline strategically targeting diseases and conditions with immense medical needs

We have developed a differentiated non-oncology pipeline of innovative biologics and small molecule assets, including four in clinical stage. Our non-oncology pipeline covers a range of diseases and conditions with large patient populations and medical needs, including RA, AA, CKD-aP, moderate-to-severe asthma, and thromboembolic disorders and others.

A223 is potentially one of the first domestically developed small molecule JAK1/2 inhibitors in China. Inhibiting JAKs, which are key mediators of multiple pro-inflammatory cytokine signals, has proven to be effective against a number of autoimmune diseases, such as RA and AA. RA is a prevalent autoimmune disease that requires long-term treatment with approximately 6.0 million patients and an RMB17.4 billion drug market in China in 2022. Inhibiting JAKs is a clinically validated approach for treating RA, with three JAK inhibitors approved by the NMPA in China for treating RA. Among them, JAK1/2 inhibitor Olumiant has been demonstrated to better improve the symptoms of RA patients based on cross-trial comparisons. However, the approved JAK inhibitors have major safety issues, with black box warning issued by the FDA for increased risks of serious side effects including serious infection, death, malignancy, thrombosis, and major adverse cardiovascular events.

A223 is configured with a structural design that retains target selectivity with optimized pharmacological properties. This potentially translates into the encouraging safety profile demonstrated by A223 in three completed trials and two ongoing trials, where most TEAEs were mild or moderate with no incidence of black box warning-related safety issues commonly reported by approved JAK inhibitors. Based on preliminary clinical data from its phase 2 trial, A223 demonstrated promising anti-rheumatic efficacy in moderate-to-severe RA patients, with A223 2 mg achieving substantial and statistically significant ACR20 difference of 35.1% (63.6% vs. 28.6%) and ACR50 difference of 33.7% (39.4% vs. 5.7%) at week 12 compared with placebo. Notably, based on non-head-to-head comparison, the ACR20 and ACR50 differences achieved by A223 2 mg are greater than those of Olumiant 4 mg, the approved dosage of Olumiant in China, in Chinese patients with moderate-to-severe RA (ACR20 difference vs. placebo: 30.8%; ACR50 difference vs. placebo: 20.7%). These promising clinical results indicates the potential of A223 to be an effective treatment option with improved

efficacy and safety for RA. Besides RA, we also target AA, a common autoimmune disease that affected approximately 4.0 million people in China in 2022. Inhibiting JAK1/2 is a clinically proven approach with Olumiant being the first and only systemic treatment approved by the FDA for severe AA and one of the only two disease-specific treatments approved in China for the same indication as of the Latest Practicable Date. We expect to complete patient enrollment of our ongoing phase 2 trial for severe AA in the second half of 2023.

In addition to A223, we are also evaluating three other clinical-stage assets (A277, SKB378 and SKB336) and various preclinical assets to target indications ranging from chronic kidney disease (CKD)-associated pruritus (CKD-aP), moderate-to-severe asthma, thromboembolic disorders, to other diseases and conditions with large patient populations and medical needs. Apart from our existing assets, we will continue to develop novel non-oncology drug candidates to address highly prevalent chronic diseases currently without effective treatments, including autoimmune and metabolic diseases.

We are also extending our ADC focus beyond cancers to non-oncology drugs for treating chronic diseases that affect a large and underserved population. For example, we are exploring novel ADCs with non-cytotoxic payloads to target autoimmune and metabolic diseases.

Integrated drug development capabilities across R&D, manufacturing, quality control and commercialization

We have developed integrated capabilities encompassing all key drug development functionalities, including R&D, manufacturing, quality control and commercialization.

Our drug development capabilities are governed by a well-established management system that covers all key business functionalities, which provides a framework for our internal teams to engage in constructive dialogues and evaluation, particularly when making critical decisions for each drug development plan. We operate a three-tiered decision-making model, consisting of: (i) a pipeline committee led by our CEO that oversees the entire lifecycle of drug development programs, (ii) discovery, CMC, and clinical development committees that serve as gatekeepers for the progress and quality of our drug development programs, and provide timely feedback in each round of planning, and (iii) project leaders that are instrumental to the effective coordination among different functional groups to ensure smooth execution of our drug development plans.

Guided by this systematic approach, our integrated drug development capabilities empower us to rapidly and strategically advance a differentiated and clinically valuable pipeline of 33 assets, including 14 in clinical stage, five in pivotal trial- or NDA registration-stage, nine in phase 1- or phase 2-stage, and nine out-license agreements as of the Latest Practicable Date.

R&D. We have a strong R&D team with rich experience and knowledge to develop our pipeline and advance our three technology platforms. Our R&D team comprises industry veterans with extensive experience of driving drug development programs at leading biopharmaceutical companies, including MNCs such as Pfizer, Wyeth, GlaxoSmithKline, Johnson & Johnson, Bristol-Myers Squibb and Novartis. Our pipeline assets are protected by a comprehensive patent portfolio, which consists of 147 issued patents, including 74 issued patents in China, 21 issued patents in the U.S. and 52 issued patents in other jurisdictions, and 255 pending patent applications as of the Latest Practicable Date.

We have a comprehensive in-house R&D engine covering drug discovery, translational medicine, process development and clinical research. Our integrated capabilities give us control and visibility over our R&D process, reduces our reliance on CROs and enable us to ensure the quality and efficiency of our drug development programs.

- *Drug Discovery*. Our drug discovery team plays a fundamental role in our development of innovative drugs to address medical needs. Our discovery team comprises medicinal chemists, computational chemists, protein scientists, biologists, immunologists and is led by experts with years of experience working at MNCs. Through bringing over ten drug candidates into clinical development, we have accumulated in-depth know-how and streamlined our drug discovery workflows for ADCs, biologics and small molecules. Our research platform support in-house capabilities covering target validation, mechanism study, candidate design and selection (including computer-aided approaches), with a goal to consistently design and engineer differentiated drug candidates with high clinical values to enrich our pipeline.

- *Translational Medicine*. Our translational medicine scientists work closely to facilitate the bridging of our drug discovery and preclinical studies with clinical needs, with an aim to bring differentiated drug candidates to market. Their interdisciplinary research encompasses a wide range of studies from drug metabolism and pharmacokinetics (DMPK), toxicology and biomarker development, to quantitative and clinical pharmacology. Our translational medicine team plays a key role in improving the success rates, time-efficiency and cost-effectiveness of our clinical trials.

- *Process Development*. Our pharmacology team is responsible for developing a quality, scalable, and robust process for our ADC, antibody and small molecule drugs. They have extensive experience in process optimization and scale-up, analytical method development, quality criteria establishment, and technology transfer. We are guided by a quality-by-design (QbD) concept to scientifically design process performance characteristics, which underlies our consistent, high-quality manufacturing of drug products.

- *Clinical Research*. We have a robust clinical research team located across our four clinical centers in Beijing, Shanghai, Chengdu and the U.S. Our clinical scientists are highly experienced at formulating clinical development plans, selecting indications, and determining regulatory pathways. Their rich experience in regulatory communication, both in China and overseas, also plays a key role in advancing our clinical development plans towards successful commercialization.

Manufacturing and Quality Control. We believe a well-established manufacturing and quality control system serves as the cornerstone of our future commercialization and underlies our ability to enhance our R&D capabilities and advance clinical development. Our manufacturing and quality control system is capable of supporting the production of antibodies, ADCs and their key drug substances. This system helps ensure the efficiency and cost-effectiveness of our clinical trials, and facilitates a smooth transition into commercial manufacturing.

- *Manufacturing*. Our main manufacturing site in Chengdu is one of the few facilities in China with cGMP-compliant, end-to-end capabilities covering the entire development lifecycle of ADCs, from cell culture and purification, antibody production, syntheses of payloads and linkers, ADC conjugation to formulation, fill and finish. In particular, our in-house cell culture and purification facilities enable us to secure quality supplies that match our specific production requirements at significantly reduced costs, supported by two 2,000 L single-use bioreactors. We are also equipped with one 300 L ADC conjugation tank with a maximum annual production capacity of 40 batches of ADC drug substance. Our new ADC formulation center is designed with an annual output of 45 batches (or 900,000 vials) of freeze-dried ADCs or 60 batches (or 1.2 million vials) of injectable ADCs.

- *Quality Control*. We operate a comprehensive quality control system which extends across all key stages of the R&D, manufacturing and commercialization processes. This system is established and refined in accordance with the rigorous regulations and guidelines in China, the U.S. and Europe. We pay close attention to the evolving cGMP standards and regulatory developments in these target markets and update our internal procedures accordingly, striving for the highest international standards in patient safety and regulatory compliance. Furthermore, our quality expert team are actively involved in the discussion and promulgation of regulations and guidelines in China, which attests to our recognized expertise in the respective fields. For example, we took an active role in the drafting of the "Biological Products (mAb)" section of the Chinese GMP Implementation Guide (Re-issued) (中國GMP實施指南(再版)《生物製品(單克隆抗體)》部分) in 2022.

Commercialization. We are well-positioned to develop our commercialization infrastructure and market access by leveraging our Controlling Shareholder Kelun Pharmaceutical's decades-long experience, industry connections and extensive network. Guided by Kelun Pharmaceutical's leading industry position, strong brand image and profound resources as one of China's largest and most established pharmaceutical companies, we are planning to develop our own commercialization team and network, with an initial focus on Class III hospitals and leading physicians across China's extensive local markets. We will also continue to refine our commercialization strategies for each late-stage drug candidate, first prioritizing therapeutic areas with medical needs in China, such as BC, NSCLC and GI cancers, while offering synergistic treatment options enabled by our diverse pipeline to optimize patient outcome.

Cross-border business development capabilities enabling collaborations and strategic partnerships

We believe that an open and collaborative mindset is crucial to the success of our global strategy. Along each step of our drug development plans – from drug discovery to commercialization – we proactively pursue external collaborations, licensing arrangements and other strategic partnerships to create synergies with our pipeline and technology platforms.

Over the years, we have established robust, cross-border business development capabilities with local presence across multiple jurisdictions, from Chengdu, Beijing and Shanghai in China to New Jersey in the U.S. Our business development team is led by seasoned professionals with decades-long experience and insights in sourcing and executing licensing deals and collaborations. They work closely with our scientists and team leaders on each project, and are involved as early as the drug discovery stage to identify and capture partnership opportunities that maximize the clinical value of our pipeline.

Our business development competencies are exemplified by a proven track record in forging strategic partnerships worldwide, which in turn reflect the increasing recognition we have received from peers and leaders in the global biopharmaceutical industry. Notably, we have successfully negotiated nine out-license agreements to date, including three license and collaboration agreements with MSD to develop up to nine ADC assets for cancer treatment. According to Frost & Sullivan, we are the first China-based company to license internally discovered and developed ADC candidates to a top-ten biopharmaceutical MNC. Our collaboration with MSD to develop up to seven preclinical ADC assets is the largest biopharmaceutical out-license deal to date secured by a China-based company, according to Frost & Sullivan, and the world's largest biopharmaceutical partnership in terms of deal value in 2022, according to Nature Reviews Drug Discovery. We have also entered into collaboration and license agreements with Ellipses for A400, and with Harbour BioMed for A167 and SKB378. Our strategic partnerships are not only testaments to our R&D and business development capabilities, but also key drivers of our continued innovation, global influence and long-term growth.

Experienced leadership backed by our Controlling Shareholder and renowned investors

We have an experienced leadership team consisting of industry veterans, regulatory experts, seasoned scientists, esteemed physicians and financial specialists. Led by our founder, Mr. Liu Gexin, and CEO, Dr. Ge Junyou, our leadership team members bring over twenty years of industry experience on average and a proven track record leading the R&D, manufacturing and commercialization of innovative drugs. Well recognized in their respective fields, they held key management roles at pharmaceutical MNCs, leading domestic biotech companies, regulatory authorities, top-grade hospitals, and renowned financial institutions.

Our leadership team is supported by a deep talent pool driving our continued innovation. As of December 31, 2022, we had 1,155 full-time employees, including 38.0% with a master's degree or above. Through our cross-functional management system and three-tiered decision-making model, key contributors from each functional group play an active role in coordinating and overseeing our drug development plans to ensure their smooth execution, enhancing overall operational efficiency. Our team members actively participate in the formulation of industry guidelines, both in China and internationally. For example, our quality control experts are members of three working groups at the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

Our Controlling Shareholder Kelun Pharmaceutical has offered invaluable guidance throughout our development, and built into our genetic fabric a shared mission to bring innovative treatments to address major medical needs. Our shareholders also consist of MSD, a top-ten MNC and one of our key strategic partners, as well as blue chip healthcare investors, including renowned global institutional investors and leading domestic investors such as IDG Capital, CMG-SDIC Capital, Lilly Asia Ventures, Hillhouse, Cinda, and Sherpa. Together, our shareholders provide us with professional insights and vital connections to the biopharmaceutical industry in China and worldwide.

OUR DEVELOPMENT STRATEGIES

Advance our indication-oriented oncology pipeline

We plan to advance the clinical development of our oncology assets, with the goal to apply for regulatory approvals and initiate product launch at the earliest time practicable. Guided by our indication-oriented approach, we will continue to advance our clinical-stage and preclinical oncology assets to target cancer indications with high prevalence and medical needs, notably BC, NSCLC and GI cancers. At the same time, we will continue to explore indication expansion and combination therapies to maximize the clinical and commercial potential of our oncology pipeline.

Full coverage of major breast cancer subtypes. We have strategically targeted BC, the most common cancer worldwide with significant underserved medical needs, as our lead oncology indication with coverage by three key assets, namely, SKB264, A166 and A167 (in combination with SKB264).

- *TNBC*. We completed patient enrollment for SKB264's pivotal phase 3 trial in advanced TNBC patients who have failed two or more lines of treatment in April 2023 and plan to submit an NDA to the NMPA by the end of 2023. We also plan to complete SKB264's phase 2 trial with or without A167 as a first-line treatment for advanced TNBC, and commence phase 3 trial in the first half of 2024.

- *HER2+ BC*. We completed patient enrollment for A166's ongoing pivotal phase 2 trial in advanced HER2+ BC patients who have failed second- or later-line treatment and submitted an NDA to the NMPA in May 2023. Pending consultation with the CDE, we also plan to initiate a confirmatory phase 3 trial of A166 as a 2L+ treatment in advanced HER2+ BC patients in the second half of 2023.

- *HR+/HER2- BC*. We are advancing the dose expansion study of SKB264's global phase 1/2 trial in advanced HR+/HER2- BC patients who have previously received at least one and no more than four lines of standard chemotherapy for metastatic disease. We completed the enrollment of this cohort in China in November 2022 and expect to advance to phase 3 in the second half of 2023.

Robust development plan for NSCLC. We are developing multiple oncology assets engineered to target different subtypes of NSCLC, the second most common cancer worldwide, with an aim to benefit patients currently without effective treatment options. In particular:

- For SKB264, we are conducting a series of clinical trials for various subtypes of NSCLC, including (i) a dose expansion study of a global phase 1/2 trial for advanced NSCLC, including advanced EGFR-wild type and EGFR-mutant NSCLC; (ii) a phase 2 trial in EGFR-mutant NSCLC patients who have failed EGFR-TKI therapy; (iii) a phase 2 trial in combination with A167 with or without chemotherapy for advanced EGFR-wild type and EGFR-mutant NSCLC, and (iv) a phase 3 trial in EGFR-mutant NSCLC patients who have failed EGFR-TKI therapy, which we expect to commence in the second half of 2023.

- In collaboration with MSD, we have commenced a phase 2 basket study of SKB264 as combination therapies (including with Keytruda, osimertinib and chemotherapy), in March 2023 in China.

- Based on the promising preliminary results of A400 in advanced RET+ NSCLC patients, we completed CDE clinical consultation and initiated a pivotal trial for 2L+ advanced RET+ NSCLC in May 2023. We also plan to commence a pivotal trial for 1L advanced RET+ NSCLC in the second half of 2023.

Expanding clinical programs for GI cancers. We are targeting GC and CRC, the two most common GI cancers worldwide. GC is the second most common cancer in China, which had approximately 43.3% of the world's GC patients in 2022, and a leading cause of cancer death globally, while CRC is the third most common cancer and a leading cause of cancer death in China. To date, we have selected GC as a key indication for both of our Core Products,

namely SKB264 and A166; and CRC as a key indication for A166 and A140. For GC, we are advancing the dose expansion study of SKB264's global phase 1/2 trial in advanced GC patients who have failed first-line treatment and a phase 1b trial of A166 for advanced HER2+ GC in China. Meanwhile, SKB315 targets CLDN18.2, which is highly expressed in GC. For CRC, we are conducting a phase 1b trial of A166 in China for advanced HER2+ CRC and a pivotal phase 3 trial of A140 in combination with chemotherapy in patients with RAS wild-type mCRC in China, for which we completed patient enrollment in November 2022 and expect to file an NDA to the NMPA in the second half of 2023.

We strive to advance the clinical development of our ADCs and other drug candidates to solidify our comprehensive coverage of major tumor types and enhance our oncology portfolio.

Besides advancing our clinical-stage oncology assets, we also seek to explore the therapeutic potential of our preclinical oncology assets for a broad range of tumor types, targeting cancers with medical needs. We will continue to leverage our in-depth expertise in tumor biology and multiple drug modalities to expand our innovative oncology programs.

Advance and expand our differentiated non-oncology drug portfolio

We will continue to build and expand our differentiated non-oncology drug portfolio to target indications with significant disease burden and medical needs, leveraging our competitive ADC, biologics and small-molecule technology platforms. For A223, our small molecule JAK1/2 inhibitor, we are conducting a phase 2 trial in patients with moderate-to-severe RA and plan to initiate a pivotal phase 3 trial in the second half of 2023. We also expect to complete patient enrollment of A223's ongoing phase 2 trial for severe AA in the second half of 2023. For A277, our peripherally-restricted KOR agonist for CKD-aP, we have completed a phase 1b clinical trial with encouraging anti-pruritic effect observed in patients on maintenance hemodialysis with moderate-to-severe CKD-aP, and we commenced a phase 2 proof-of-concept trial in September 2022. We will also continue to advance the clinical development of our two early-stage drug candidates SKB378 and SKB336.

In addition, we will continue to develop novel non-oncology drug candidates to address highly prevalent chronic diseases currently without effective treatments, including autoimmune and metabolic diseases. These chronic diseases are often associated with aging and exacerbated by the complex interactions of numerous lifestyle and environmental factors. We are dedicated to designing novel drug candidates and promoting R&D innovations to address these and other medical needs.

Enhance our integrated drug development capabilities

R&D. In addition to expanding our drug portfolio, we are dedicated to optimizing our R&D platforms and developing novel technologies to support the R&D of next-generation drugs. In particular, leveraging our experience and data from drug discovery, translational medicine, process development and clinical studies over years of implementing our ADC design strategies, we deploy a multi-pronged strategy to advance our ADC platform, including

(i) further optimizing our payload/linker technologies to solidify our ADC capabilities; (ii) developing bsADCs equipped with dual-targeting antibodies to deliver enhanced clinical benefits; (iii) developing other novel ADC designs such as iADCs, RDCs, dual-payload ADCs; and (iv) developing ADCs with non-cytotoxic payloads to target non-oncology diseases. Besides developing new forms of drug conjugation, we are exploring PROTAC technology, a novel method to generate small molecules with the potential to induce degradation of a target protein. We aim to improve the therapeutic value and drug-like properties of the resulting PROTAC molecules through in-depth target biology research, CADD, enhanced preclinical safety evaluation methods, and other techniques that help optimize the discovery process.

Manufacturing and Quality Control. We will continue to expand our cGMP facilities to support the anticipated commercialization of our near-commercial assets. For our cell culture and purification unit, we plan to install one additional 2,000 L single-use bioreactor, bringing our total in-house capacity to 6,000 L. Going forward, we will continue to enhance our manufacturing capabilities, both through expanding our in-house capacity and through collaborating with industry-recognized CMOs. Meanwhile, we strive to upgrade and improve our comprehensive quality control system, benchmarking against the highest international standards adopted by pharmaceutical MNCs, to ensure patient safety and regulatory compliance.

Commercialization. Based on the expected approval timeline of each late-stage project in our pipeline, we expect to receive conditional marketing approval from the NMPA for A167 (PD-L1 mAb), our first innovative drug in NDA registration stage, in the second half of 2023 or the first half of 2024. Subject to regulatory communications and marketing approval, we expect to launch our Core Products, SKB264 and A166, and A140 in the China market in the second half of 2024 or the first half of 2025. In anticipation of these upcoming milestones, we are actively recruiting talents with a strong background in oncology, especially in BC, NSCLC, GI cancers and NPC, our lead indications for these late-stage assets. We plan to set up a fully-fledged commercialization team by the end of 2023 to oversee and coordinate the sales and marketing of A167, as well as the pre-marketing preparation for SKB264 and A166, laying the groundwork for rapid commercial-scale distribution upon these two ADCs' anticipated NDA approval by the NMPA. Globally, we will continue to pursue a flexible strategy to capture the commercial value in major international markets, through forging synergistic license and collaboration opportunities worldwide.

Continue to seek and deepen strategic partnerships to extend the potential of our technology platforms and maximize the value of our pipeline

Following on the success of our existing license and collaboration agreements, we are actively exploring new partnership opportunities globally. We take a two-pronged business development approach to drive both our near- and long-term growth: for clinical-stage assets, we focus on forging partnerships with MNCs and leading domestic companies to accelerate our development timelines and maximize the commercial value of our pipeline; for early-stage assets and drug discovery, we seek co-development opportunities that enable us to explore new therapeutic areas and cutting-edge modalities, such as PROTAC and RDCs, and augment our

technology platforms. Meanwhile, we are closely monitoring global opportunities to in-license new drug candidates and innovative technologies that could bring strategic synergies to our pipeline and technology platforms. We will consider whether to retain the Greater China commercial rights of, or fully out-license, our assets as we evaluate opportunities on a case by case basis. We are also committed to enhancing our collaborations with KOLs, top hospitals and academic institutions, in China and globally, to ensure our timely access to cutting-edge research and support our existing and future pipeline.

Optimize our integrated operation system to become a leading global biopharmaceutical company

We are continuously reviewing and optimizing our internal procedures, particularly our R&D management process, to enhance operational efficiency and support our growth as a fully fledged biopharmaceutical company. We also aim to attract and recruit outstanding scientific, marketing and managerial personnel to join our talent pool, in order to maintain our competitiveness in a rapidly evolving industry.

Meanwhile, we are actively seeking opportunities to expand our global footprint and raise international brand awareness. As our business continues to grow, we will adhere to our mission to address major medical needs in China and globally, and to bring world-class treatments, and a healthier and happier life, to all patients.

OUR PIPELINE

Our pipeline targets the world's prevalent or hard-to-treat cancers, such as BC, NSCLC and GI cancers, as well as non-oncology diseases and conditions affecting a large and underserved population. As of the Latest Practicable Date, we had established a pipeline of 14 clinical-stage drug candidates, including five in pivotal trial- or NDA registration-stage. We have also assembled a diverse portfolio of preclinical assets, including four in IND-enabling stage, to further enrich our expanding pipeline targeting medical needs.

The clinical value of our pipeline and our drug development capabilities are recognized by the strategic partnerships we have forged worldwide to unlock the global market potential of key assets. To date, we have entered into nine out-license agreements, including three license and collaboration agreements with MSD to develop up to nine ADC assets for cancer treatment. We have also entered into collaboration and license agreements with Ellipses for A400, and with Harbour BioMed for A167 and SKB378. Our strategic partnerships are not only testaments to our R&D and business development capabilities, but also key drivers of our continued innovation, global influence and long-term growth.

The pipeline chart below summarizes the development status of our clinical-stage drug candidates and selected preclinical assets.

Abbreviations: TNBC: triple-negative breast cancer; BC: breast cancer; NSCLC: non-small-cell lung cancer; NPC: nasopharyngeal cancer; GC: gastric cancer; OC: ovarian cancer; SCLC: small-cell lung cancer; UC: urothelial cancer; HNSCC: head and neck squamous cell carcinoma; EC: endometrial cancer; CRPC: castration-resistant prostate cancer; CRC: colorectal cancer; MTC: medullary thyroid cancer; CKD-aP: chronic kidney disease-associated pruritus

Notes: 1. Including immunotherapy and targeted therapies; 2. No phase II clinical trial is required for biosimilar drug candidates in China; 3. CDE consultation completed; 4. We completed a phase 1a study and are conducting a phase 1b study. Based on the NMPA's approval, we also commenced a pivotal phase 2 clinical trial. Upon meeting the primary endpoint in this trial, we filed NDA for conditional approval, which is under priority review. Although we completed the study per protocol, the trial is ongoing as certain patients responsive to the drug continue with treatment. Pending consultation with the CDE, we plan to commence a confirmatory phase 3 trial in 2H 2023; 5. CDE consultation ongoing; 6. A phase 1a and pivotal phase 2 clinical trial was completed. We commenced a confirmatory phase 3 trial upon consultation with the CDE; 7. Phase 1a/1b trial.

Oncology Franchise – ADCs

SKB264 – A Novel TROP2 ADC, Our Core Product

Overview

SKB264 is a novel, internally discovered and developed TROP2 ADC targeting advanced solid tumors. Drugs that successfully target TROP2 have vast market potential as TROP2 is frequently overexpressed across a broad spectrum of cancers, especially in highly prevalent or hard-to-treat cancers such as BC, NSCLC, GC and OC. The global TROP2 ADC market is expected to increase from US$0.7 billion in 2022 to US$25.9 billion by 2030, representing a CAGR of 57.6%, while the TROP2 ADC market in China, following the NMPA approval of the first TROP2 ADC in June 2022, is projected to grow from RMB0.2 billion in 2023 to RMB23.6 billion by 2030 at a CAGR of 103.0%.

Positioned to be the first domestically developed TROP2 ADC in China, SKB264 utilizes a differentiated drug design to improve ADC stability and maintain ADC bioactivity, thus enhancing its targeting ability and reducing its off-target and on-target off-tumor toxicity, potentially leading to a broader therapeutic window. Preliminary clinical data from SKB264's global phase 1/2 trial showed that SKB264 demonstrated encouraging ORRs across multiple types of heavily pretreated advanced solid tumors, highlighted by an ORR of 43.6%, 42.9% and 43.6% in heavily pre-treated TNBC, HR+/HER2- and NSCLC patients, respectively. SKB264 also demonstrated a potentially favorable safety profile. Based on non-head-to-head cross-trial comparisons, SKB264 demonstrated lower incidences of decreased neutrophil count (54% vs 78% for all grades, 26% vs 49% for ≥ grade 3) and diarrhea (4% vs 59% for all grades, 0% vs 11% for ≥ grade 3) compared with Trodelvy; and no incidence of treatment-related ILD compared with that reported in DS-1062-treated patients (6% for all grades and 2% for ≥ grade 3). We are also exploring SKB264's early-line potential in combination therapy. Based on preliminary results from a phase 2 trial conducted in China, SKB264 in combination with A167 demonstrating a promising ORR of 85.7% as a first-line therapy in advanced TNBC patients.

Supported by its promising proof-of-concept results, SKB264 was granted Breakthrough Therapy Designation by the NMPA for advanced TNBC in July 2022 and for EGFR-TKI failed EGFR-mutant advanced NSCLC in January 2023. In May 2022, we granted MSD exclusive development and commercialization rights for SKB264 outside Greater China. See "– Our License and Collaboration Arrangements – License and Collaboration Agreement with MSD for SKB264" for details.

We are actively advancing a multi-strategy clinical development plan to explore SKB264's potential as a monotherapy and combination therapies to treat various types of advanced solid tumors:

- Breast Cancer. SKB264 targets TNBC and HR+/HER2- BC, two major subtypes of BC, the most common cancer worldwide. We commenced a pivotal phase 3 trial in advanced TNBC patients in April 2022, which enables SKB264 to become the first

domestically developed TROP2 ADC to enter the pivotal stage, as well as a phase 2 trial of SKB264 monotherapy or in combination with A167, our PD-L1 mAb, as first-line treatment for advanced TNBC. We are also advancing the dose expansion study of SKB264's global phase 1/2 trial in advanced HR+/HER2- BC patients.

- NSCLC. We are conducting a dose expansion study in advanced NSCLC patients (including EGFR-mutant NSCLC and EGFR-wild type NSCLC) as part of SKB264's global phase 1/2 trial, and initiated a phase 2 trial of SKB264 in combination with A167 with or without chemotherapy as an early-line treatment for NSCLC in China in May 2022. Moreover, we are collaborating with MSD on a phase 2 basket study of SKB264 as combination therapies (including with Keytruda, osimertinib and chemotherapy) for advanced EGFR-wild type and EGFR-mutant NSCLC, which we commenced in March 2023 in China.

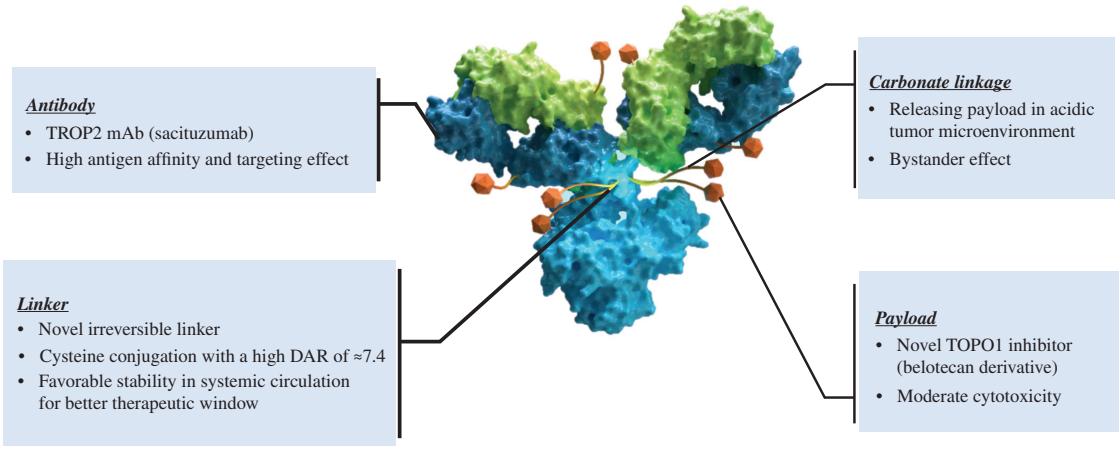
- Other Major Cancers. We are actively exploring the potential of SKB264 both as a monotherapy and as combination therapies for treating other major indications, including advanced GC and OC, for which no TROP2 ADCs were approved globally as of the Latest Practicable Date and where we may have a potential fast- or first-to-market advantage. We are collaborating with MSD on a global phase 2 basket study of SKB264 in combination with Keytruda for selected solid tumors, including recurrent or metastatic CC, advanced UC, recurrent OC and metastatic prostate cancer.

For details, see "– Our Pipeline – Oncology Franchise – ADCs – SKB264 – Clinical Development Plan."

Drug Design and Mechanism of Action

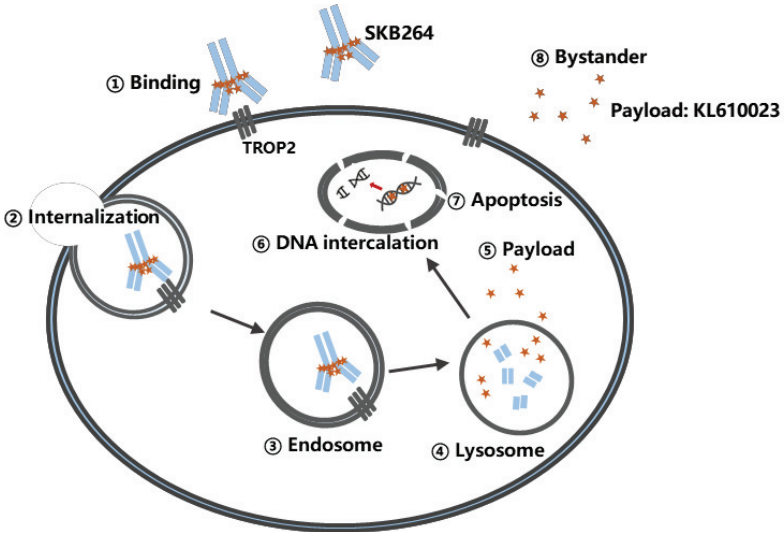
TROP2 is a calcium signal transducer protein that spans the cellular membrane. TROP2 overexpression has been reported in many epithelial cancers, particularly in several prevalent or hard-to-treat cancers including BC, NSCLC, GC and OC, and is associated with tumor aggressiveness, progression, and metastasis. Given its overexpression in a wide range of tumors and low expression in normal cells, TROP2 has emerged as a promising cancer drug target.

TROP2-directed therapies require complex drug design to minimize potential systemic toxicity in TROP2-expressing normal tissues. Leveraging our ADC platform and expertise, SKB264 is designed to improve upon the first FDA-approved TROP2 ADC, Trodelvy, with its core components and innovative features illustrated below.



SKB264 features a moderate payload toxicity-high DAR design, in which KL610023, a novel belotecan-derivative topoisomerase I (TOPO1) inhibitor with moderate cytotoxicity, is conjugated at a high DAR to sacituzumab, a clinically proven TROP2 mAb. Our proprietary drug-linker strategy, *Kthiol*, is used to improve ADC stability and reduce off-target and on-target off-tumor toxicity. The use of a novel carbonate linkage, which connects the antibody and payload, exploits the acidic tumor microenvironment to selectively release cytotoxic payloads in tumor tissues, thereby facilitating internalization of payloads by tumors cells and subsequent intracellular tumor killing, as well as bystander killing when payloads permeate out of ADC-targeted cells and diffuse into neighboring tumor cells. For details regarding *Kthiol*, see "– Our Technology Platforms – ADC Platform."

Mechanistically, sacituzumab directs SKB264 selectively to TROP2-expressing tumor cells. The acid-cleavable linker then exploits the acidic pH in both the intracellular lysosome and the extracellular tumor microenvironment, releasing KL610023 both intracellularly once it is internalized by the tumor cells and extracellularly to the tumor microenvironment. The high membrane permeability of KL610023 allows KL610023 to permeate into bystander cells to which SKB264 has not bound, regardless of their TROP2 expression status. Intracellularly, KL610023 inserts itself into the DNA structure i.e., intercalation, and inhibits TOPO1, an enzyme essential to DNA replication. Inhibition of TOPO1 leads to DNA damage during the replication process, causing apoptosis. In this way, SKB264 elicits both targeted killing in TROP2-expressing tumor cells and bystander killing in TROP2-negative tumor cells, which helps overcome heterogeneity in tumors where there is uneven expression of TROP2. The diagram below illustrates the mechanism of action of SKB264:



Market Opportunity and Competition

SKB264 has vast market potential as TROP2 is frequently overexpressed across a broad spectrum of cancers, such as BC (TNBC and HR+/HER2- BC), NSCLC, GC and OC. In May 2022, we out-licensed the development and commercialization rights for SKB264 outside Greater China to MSD, with whom we are closely collaborating on SKB264's global clinical development.

The global TROP2 ADC market is expected to increase from US$0.7 billion in 2022 to US$25.9 billion by 2030, representing a CAGR of 57.6%. Following the NMPA approval of the first TROP2 ADC in June 2022, the TROP2 ADC market in China is projected to grow from RMB0.2 billion in 2023 to RMB23.6 billion by 2030 at a CAGR of 103.0%. For more details regarding the addressable market size of TROP2 ADCs, see "Industry Overview – Global and China's TROP2 ADC Markets – Addressable Market Size of TROP2 ADCs."

The following table summarizes the major indications targeted by SKB264.

Disease indication	Subtype	Treatment paradigm	Positioning of SKB264[1]
BC	TNBC	First-line: single-agent or doublet chemo, chemoimmunotherapy, PARPi	3L+ (mono)
		Later-line: Trodelvy	1L (combo)
	HR+/HER2- BC	First-line: doublet endocrine therapy, combination endocrine therapy with PI3Ki/mTORi/chidamide	2L+ (mono)
		Later-line: Trodelvy (U.S.-only)	

Disease indication	Subtype	Treatment paradigm	Positioning of SKB264[1]
NSCLC	EGFR-mutant NSCLC	First-line: TKI	1L (combo)
		Later-line: platinum-based doublet chemo with or without bevacizumab, single-agent chemo, PD-(L)1 inhibitor	2/3L (mono) TKI failure (mono and combo)
	EGFR-wild type	First-line: chemoimmunotherapy with or without bevacizumab, doublet chemo with or without PD-(L)1 inhibitor, PD-(L)1 monotherapy	1L (combo)
		Later-line: PD-(L)1 inhibitor monotherapy, single-agent chemo, multi-targeting TKI	
GC	N/A	First-line HER2+: combination chemo with trastuzumab, PD-1 inhibitor (PD-L1-positive only)	2L+ (mono)
		Later-line HER2+: similar to that of HER2- GC with the addition of combination chemo with trastuzumab, HER2 ADC Aidixi (China-only)	
		First-line HER2-: doublet or triplet chemo, PD-1 inhibitor (PD-L1-positive only)	
		Later-line HER2-: single-agent chemo, other chemo regimens, PD-1 inhibitor, apatinib	
OC	Recurrent and metastatic OC	First-line: debulking surgery with platinum doublet chemo with or without bevacizumab	2L maintenance (combo)
		Later-line platinum-sensitive: platinum doublet chemo, bevacizumab, PARPi, PD-1 inhibitor, non-platinum chemo	
		Later-line platinum-resistant: non-platinum chemo, bevacizumab, PARPi, PD-1 inhibitor	

Note:

(1) In the China market.

TNBC. BC is the most common cancer worldwide. TNBC is an aggressive subtype of BC, accounting for about 15% of total BC cases. According to Frost & Sullivan, the global incidence of TNBC increased from 306.7 thousand in 2017 to 352.2 thousand in 2022 and is expected to reach 408.8 thousand in 2030, while the incidence of TNBC in China grew from 47.3 thousand in 2017 to 51.2 thousand in 2022 and is anticipated to reach 55.6 thousand in 2030. Approximately 85% of TNBC patients are diagnosed with advanced disease, with a five-year survival rate of about 12%.

The treatment paradigm for advanced TNBC in the U.S. and China primarily involves single-agent or doublet chemotherapy, chemoimmunotherapy that combines chemotherapy with PD-1 inhibitor (for PD-L1+ patients) and PARP inhibitor (for patients with deleterious BRCA mutations) in the front-line setting, and TROP2 ADC Trodelvy in the late-line setting. Despite the greater survival benefits provided by chemoimmunotherapy and PARP inhibitor for PD-L1+ patients and patients with deleterious BRCA mutations, respectively, PD-L1 expression (20%) and BRCA1/2 mutations (10-20%) are only present in a subset of advanced TNBC patients, underscoring a significant unmet need for therapies that can potentially treat a broader patient population. TROP2 is thus an attractive drug target for monotherapy and combination therapy, as it is overexpressed in about 88% of TNBC patients.

Although the recent approval of Trodelvy (TROP2 ADC) as a third-line and beyond (3L+) treatment improves survival in heavily pre-treated patients with advanced TNBC, many patients are unresponsive or develop resistance to Trodelvy. Moreover, the FDA issued a black box warning for Trodelvy for severe neutropenia (i.e., a lower-than-normal number of neutrophils in the blood) and severe diarrhea. Consequently, there is a substantial unmet need for safe and effective treatments. As of the Latest Practicable Date, according to Frost & Sullivan, Trodelvy was the only TROP2-directed drug approved for the treatment of advanced TNBC in the U.S. and China, and there were two TROP2 ADC candidates in phase 3 clinical trials for TNBC in the U.S. and two in China. For details of the competitive landscape of TROP2 ADCs, see "Industry Overview – Global and China's TROP2 ADC Markets – Competitive Landscape of TROP2 ADCs in the U.S. and China."

HR+/HER2- BC. HR+/HER2- BC is the most prevalent subtype of BC, accounting for about 55% of all BC cases. According to Frost & Sullivan, the global incidence of HR+/HER2- BC grew from 1.1 million in 2017 to 1.3 million in 2022 and is expected to reach 1.5 million in 2030, while the incidence of HR+/HER2- BC in China rose from 173.4 thousand in 2017 to 187.6 thousand in 2022 and is anticipated to reach 203.8 thousand in 2030. About 5-10% of HR+/HER2- BC patients are diagnosed with advanced disease, with a five-year survival rate of about 30%.

Endocrine therapy represents the mainstay treatment for advanced HR+/HER2- BC in the U.S. and China. However, it is estimated that 40-50% of advanced HR+/HER2- BC patients are resistant to endocrine therapy. Patients refractory to endocrine therapy currently have limited effective treatment options available, leaving a significant unmet need for effective non-endocrine therapy-based treatment. Given that TROP2 is frequently overexpressed in HR+/HER2- BC, ADCs targeting TROP2-expressing tumor cells represent a promising therapeutic strategy. As of the Latest Practicable Date, according to Frost & Sullivan, Trodelvy was the only TROP2 ADC approved for treating advanced HR+/HER2- BC in the U.S., and there was no TROP2 ADC approved for the same indication in China. There was one TROP2 ADC candidate in phase 2 or beyond for HR+/HER2- BC in the U.S. and two in China. For further details, see "Industry Overview – Global and China's TROP2 ADC Markets – Competitive Landscape of TROP2 ADCs in the U.S. and China."

NSCLC. Lung cancer (LC) is the second most common cancer and the leading cause of cancer death worldwide. NSCLC represents the predominant subtype of LC and accounts for over 85% of all LC cases. According to Frost & Sullivan, the global incidence of NSCLC rose from 1.7 million in 2017 to 2.0 million in 2022 and is anticipated to reach 2.5 million in 2030, while the incidence of NSCLC in China increased from 714.2 thousand in 2017 to 836.8 thousand in 2022 and is projected to reach 1.1 million in 2030. Approximately 55% of NSCLC patients are diagnosed with advanced disease.

The treatment paradigm of advanced NSCLC in the U.S. and China can be broadly classified based on the presence or absence of actionable driver mutations, i.e., genetic mutations that drive cancer development. For driver mutation-positive advanced NSCLC, targeted therapies directed against specific actionable driver mutations, typically TKIs, are usually considered in the 1L setting. For patients who have failed TKIs, platinum-based doublet chemotherapy with or without anti-angiogenic mAb bevacizumab, single-agent chemotherapy, or PD-(L)1 inhibitor monotherapy is usually considered. For driver mutation-negative advanced NSCLC, the 1L treatment options include chemoimmunotherapy with or without bevacizumab, doublet chemotherapy with or without PD-(L)1 inhibitor, and monotherapy with PD-(L)1 inhibitor (for PD-L1+ patients). 2L+ treatment options include PD-(L)1 inhibitor monotherapy, single-agent chemotherapy, and multi-targeting TKI anlotinib (for patients who have failed two chemotherapy regimens).

Despite the available treatment options, the five-year survival rates for advanced NSCLC patients in the U.S. and China are only about 8% and less than 5%, respectively. Although the recent addition of PD-(L)1 inhibitors to standard treatments has improved the survival of patients with driver mutation-negative advanced NSCLC, many patients remain unresponsive. Meanwhile, each TKI is only clinically relevant for a subset of advanced NSCLC patients with a specific driver mutation, with an ORR ranging from 30.0-93.0%. As TROP2 is overexpressed broadly in NSCLC, TROP2 ADCs represent a promising modality for treating advanced NSCLC regardless of driver mutation status. Moreover, as ADCs are able to deliver high doses of cytotoxic payload selectively to tumor cells with reduced damage to healthy cells, they can potentially offer improved efficacy and safety compared with chemotherapy in the 1L setting, when combined with PD-(L)1 inhibitors in chemoimmunotherapy regimens. As of the Latest Practicable Date, there were no TROP2 ADCs approved for treating advanced NSCLC in the U.S. and China, and there were two TROP2 ADC candidates in phase 3 clinical trials for NSCLC in the U.S. and one in China. For further details, see "Industry Overview – Global and China's TROP2 ADC Markets – Competitive Landscape of TROP2 ADCs in the U.S. and China."

GC. GC is the sixth most common and the third most deadly cancer worldwide. According to Frost & Sullivan, the global incidence of GC grew from 1.0 million in 2017 to 1.2 million in 2022 and is forecasted to reach 1.4 million in 2030. According to the same source, China is one of the countries with the highest incidence of GC, accounting for approximately 44% of GC incidence in the world. The incidence of GC in China increased from 429.0 thousand in 2017 to 498.6 thousand in 2022 and is expected to reach 619.6 thousand in 2030. Approximately 40-50% of GC patients are diagnosed with advanced disease.

The standard treatments of advanced GC in the U.S. and China comprises chemotherapy, targeted therapy such as anti-HER2 drugs and anti-angiogenic drugs, and PD-1 inhibitors. Advanced GC patients have a poor overall prognosis, with a five-year survival rate of less than 10% in both the U.S. and China, as there are limited targeted drugs available and immunotherapy has only modest efficacy. Consequently, there is a significant unmet need for innovative targeted therapies. Given that TROP2 is overexpressed in approximately 56% of GC, ADCs targeting TROP2-expressing tumor cells represent a promising therapeutic strategy. As of the Latest Practicable Date, there were no TROP2 ADCs approved for treating advanced GC in the U.S. and China, and there was one TROP2 ADC candidate in phase 2 clinical trial for GC only in the U.S. For further details, see "Industry Overview – Global and China's TROP2 ADC Markets – Competitive Landscape of TROP2 ADCs in the U.S. and China."

OC. OC is the third most common and the fifth deadliest cancer of the female reproductive system worldwide. According to Frost & Sullivan, the global incidence of OC rose from 289.3 thousand in 2017 to 326.4 thousand in 2022 and is anticipated to reach 379.9 thousand in 2030, while the incidence of OC in China increased from 52.0 thousand in 2017 to 57.0 thousand in 2022 and is expected to reach 62.4 thousand in 2030. Approximately 70% of OC patients are diagnosed with advanced disease.

Chemotherapy represents the cornerstone treatment for advanced OC in the U.S. and China. Despite standard treatments, the prognosis of advanced OC patients remains poor, with a five-year survival rate of about 30% in the U.S. and around 30-40% in China. Given that TROP2 is overexpressed in approximately 59% of OC, TROP2 ADCs targeting TROP2-expressing tumor cells represent a promising therapeutic strategy. As of the Latest Practicable Date, there were no anti-TROP2 ADCs approved for treating advanced OC in the U.S. and China, and there were two TROP2 ADC candidates in phase 2 or beyond for OC in the U.S. and one in China. For further details, see "Industry Overview – Global and China's TROP2 ADC Markets – Competitive Landscape of TROP2 ADCs in the U.S. and China."

Competitive Advantages

SKB264 is a novel TROP2 ADC targeting advanced solid tumors. We believe SKB264 has the following competitive advantages:

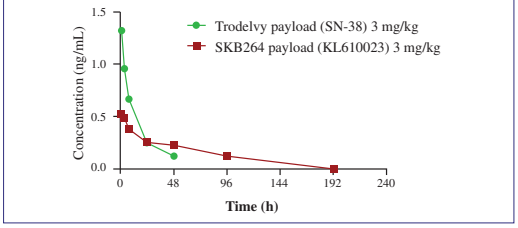
Differentiated Drug Design that Potentially Improves Therapeutic Window. SKB264 is designed with a moderately toxic payload that potentially limits toxicities to normal TROP2-expressing cells. Its high DAR enables more payload molecules to be delivered to the tumor site than systemic chemotherapy can achieve, thus potentially preventing TROP2-expressing tumor cells from repairing DNA damage.

The structure of both the payload and linker used in SKB264 contributed to increased ADC stability, thus maintaining ADC bioactivity. We used *Kthiol*, our proprietary drug-linker strategy, to improve ADC stability and reduce off-target and on-target off-tumor toxicity. Unlike the reversible addition of maleimide to cysteine in Trodelvy, the linker of SKB264 is coupled with methylsulfonyl pyrimidine as an adaptor via an irreversible covalent binding with

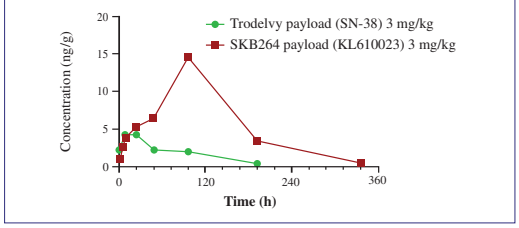
disulfide reduced cysteine. This prevents the payload from falling off easily from the ADC in circulation. Moreover, the chemical structure of toxic payload KL610023, a belotecan-derivative TOPO1 inhibitor, also contributes to the improved stability of SKB264 in circulation. Once reaching tumor sites, the carbonate cleavage moiety in the linker allows efficient payload release to exert killing effect. This innovative design enhances the targeting ability of SKB264 while reducing its off-target and on-target off-tumor toxicity, thereby potentially leading to a broader therapeutic window.

We evaluated the anti-tumor efficacy, safety and PK properties of SKB264 alongside approved TROP2 ADC Trodelvy in a cell-line derived xenograft (CDX) model, in which immunodeficient mice were implanted with HCC1806, an established human TNBC cell line. As illustrated in the diagrams below, compared with Trodelvy at the same dose (3 mg/kg), SKB264 exhibited a comparable level of payload exposure in plasma but about 4.6 times higher payload exposure in tumor tissue, suggesting that SKB264 is more efficient in releasing cytotoxic payload in the tumor.

Plasma Concentration-Time Curve of KL610023 & SN38

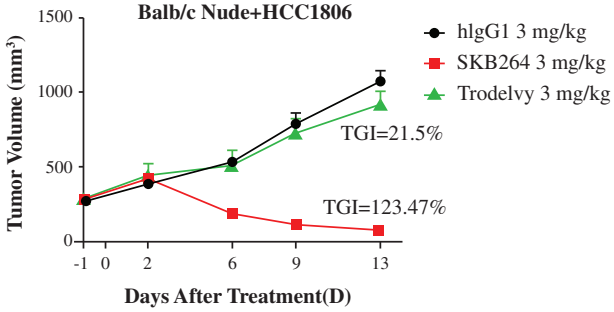


Tumor Concentration-Time Curve of KL610023 & SN38



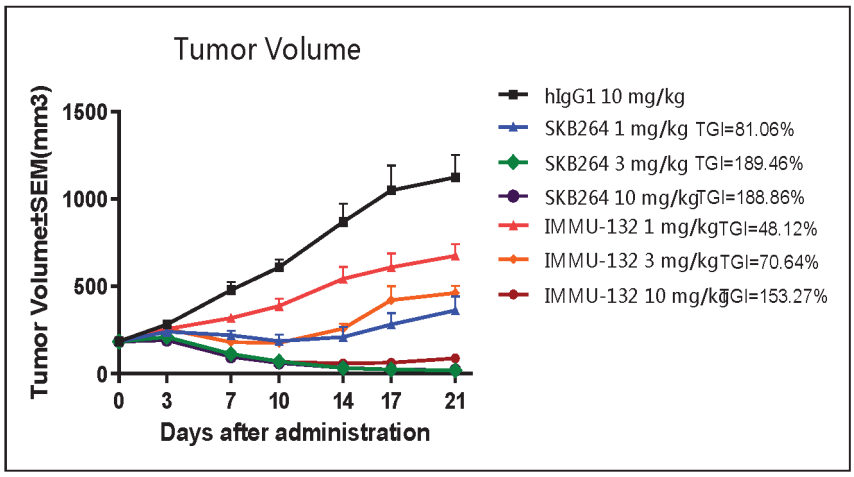
This indicates SKB264 may have a higher anti-tumor potency, evidenced by the 123.47% TGI achieved by SKB264 compared to 21.5% by Trodelvy at the same dose 13 days after treatment in a head-to-head study with Trodelvy using the HCC1806 CDX model, as shown in the diagram below. The larger intra-tumor exposure of SKB264 accounted for the greater TGI, indicating SKB264's potentially greater effectiveness in cancer treatment.

Tumor Volume Changes in CDX Mice Model (IV Admin.)



In another head-to-head study with Trodelvy using the same CDX model, treatment with SKB264 resulted in superior TGI on day 21 compared to Trodelvy at the same dose for all three doses (1, 3 and 10 mg/kg) tested in the study, as shown in the diagram below. Notably, the TGI

achieved by 3 mg/kg of SKB264 was greater than that achieved by 10 mg/kg of Trodelvy, suggesting that SKB264 can be administered at a lower dose to minimize adverse effects while providing comparable, if not better, efficacy.



Promising Anti-tumor Activity. The differentiated drug design of SKB264 potentially contributes to its promising anti-tumor activity, supported by the preliminary clinical data from SKB264's global phase 1/2 trial. According to the latest non-head-to-head data publicly available, SKB264 demonstrated encouraging ORRs compared with Trodelvy and DS-1062 (a phase 3-stage TROP2 ADC) as monotherapy for treating multiple types of heavily pretreated advanced solid tumors, as shown in the table below. Based on its promising proof-of-concept results, SKB264 was granted Breakthrough Therapy Designation by the NMPA for advanced TNBC in July 2022 and for EGFR-TKI failed EGFR-mutant advanced NSCLC in January 2023.

Although no head-to-head data are available at this stage, we believe the following comparisons shed light on the differentiated features and advantages of SKB264 from an efficacy perspective.

		ORR	
Tumor type	**SKB264**	**Trodelvy**	**DS-1062**
TNBC[1]	43.6%	35%	32%
HR+/HER2- BC[2]	42.9%	21%	27%
EGFR-mutant NSCLC[3]	60.0%	N/A	35%
EGFR-wild type NSCLC[4]	26.3%	17%	28%

Sources:

(1) Trodelvy: ESMO2020; DS-1062: SABCS21

(2) Trodelvy: ASCO2022; DS-1062: SABCS2022

(3) DS-1062: ESMO 2021 (Data based on 34 NSCLC patients with actionable genomic alterations including 29 with EGFR mutations)

(4) Trodelvy: A. Bardia, Ann Oncol 2021; DS-1062: WCLC 2021 (Data based on 50 NSCLC patients among which 84% had EGFR-wild type NSCLC)

Potentially Favorable Safety Profile. The differentiated payload/linker design and conjugation strategy of SKB264 to reduce safety risk was reflected by the encouraging safety profile of SKB264 in clinical trials. As of the data cut-off date (August 21, 2022) and at the recommended phase 2 dose (RP2D) (5 mg/kg, Q2W) in the dose expansion cohorts from SKB264's global phase 1/2 trial, grade 3 or above TRAEs were reported in 99 (52.7%) patients. Treatment-related serious adverse events (TRSAEs) occurred in 51 (24.2%) patients, and no TRAEs leading to death was reported.

The table below summarized the most commonly observed AEs by preferred terms for SKB264 and non-head-to-head cross-trial comparisons with Trodelvy and DS-1062. Compared with Trodelvy, SKB264 demonstrated lower incidences of decreased neutrophil count (54% vs 78% for all grades, 26% vs 49% for ≥ grade 3) and diarrhea (4% vs 59% for all grades, 0% vs 11% for ≥ grade 3). No incidence of treatment-related ILD was reported in SKB264-treated patients, compared with that reported in DS-1062-treated patients (6% for all grades and 2% for ≥ grade 3). Although no head-to-head data are available at this stage, we believe the following comparison sheds light on the differentiated features and advantages of SKB264 from a safety perspective.

Common adverse drug reaction incidences[1] for SKB264, Trodelvy and DS-1062

	SKB264 5mg/kg (N=188)		Trodelvy 10mg/kg (N=258)		DS-1062 6mg/kg (N=50)	
Preferred Term	**All grades**	**≥ Grade 3**	**All grades**	**≥ Grade 3**	**All grade**	**≥ Grade 3**
Hematology laboratory abnormalities						
Decreased neutrophil count	54%	26%	78%	49%	N/A	N/A
Decreased hemoglobin	72%	23%	94%	9%	N/A	N/A
Decreased platelet count	32%	8%	23%	1.2%	N/A	N/A
Decreased leukocyte count	59%	17%	86%	41%	N/A	N/A
Decreased lymphocyte count	18%	4%	88%	31%	N/A	N/A
Lung-related AEs						
ILD	0%	0%	N/A	N/A	6%	2%
GI-related AEs						
Diarrhea	4%	0%	59%	11%	16%	0%
Stomatitis	44%	9%	17%	2%	60%	2%
Nausea	31%	1%	57%	3%	64%	4%
Vomiting	27%	0.5%	33%	2%	18%	0%
Constipation	5%	0%	37%	0.4%	22%	0%
Abdominal pain	2%	0%	30%	3%	N/A	N/A
Other AEs						
Rash	35%	4%	12%	0.4%	8%	0%
Alopecia	32%	0%	47%	0%	42%	0%
Decreased appetite	18%	1%	28%	2%	26%	2%

Notes:

(1) This table summarizes the common drug adverse reactions (≥30% all grades or ≥2% grades 3 or 4) for SKB264, Trodelvy, or DS-1062.

Source: DS-1062: WCLC 2021; Trodelvy: Trodelvy's drug label.

For further details on the efficacy and safety of SKB264 in the global phase 1/2 trial, see "– Our Pipeline – Oncology Franchise – ADCs – SKB264 – Summary of Clinical Trial Data – Phase 1/2 First-in-human Clinical Trial for Selected Advanced Solid Tumors."

Significant Early-line Potential in Combination Therapy. ADCs in combination with immune checkpoint inhibitors, such as PD-(L)1 mAbs, have the potential to improve clinical outcome. The mechanisms of action of SKB264 potentially synergize with PD-(L)1 mAbs by drawing T cells towards the tumor site, thereby facilitating immune checkpoint inhibition and exposing tumor cells to immune attacks. Our combination strategies for SKB264, including with A167 and Keytruda, potentially allow us to expand into earlier treatment lines with greater efficacy in a wide range of indications, starting from advanced TNBC and advanced NSCLC. Based on preliminary results from a phase 2 trial conducted in China, SKB264 with A167 demonstrated a promising ORR of 85.7% as a first-line treatment in advanced TNBC patients. According to the latest non-head-to-head data publicly available, Keytruda in combination with carboplatin-based doublet chemotherapy, the existing standard treatment, had an ORR of 40.8% in first-line advanced TNBC patients in a phase 3 trial.

Clinical Development Plan

We are advancing the clinical development of SKB264 with the aim to be the first domestically developed TROP2 ADC approved in China. We have adopted the following development strategies for SKB264:

Fast-to-market Monotherapy Strategy for Major Indications of Interest. Currently, patients with advanced TNBC who progressed on standard treatment have limited options, with Trodelvy being the only ADC approved in China as a 3L+ treatment as of the Latest Practicable Date. SKB264 has the potential to address this medical need based on its promising efficacy data and favorable safety profile in advanced TNBC patients. This is supported by the preliminary clinical data from SKB264's global phase 1/2 trial, based on which SKB264 was granted Breakthrough Therapy Designation by the NMPA in July 2022. We commenced patient enrollment for a pivotal phase 3 trial in advanced TNBC patients in August 2022, enabling SKB264 to become the first domestically developed TROP2 ADC to enter the pivotal stage. We anticipate to complete patient enrollment for this pivotal trial in the second half of 2023 and submit an NDA to the NMPA by the end of 2023.

We are also advancing the dose expansion study in advanced HR+/HER2- BC patients and advanced NSCLC patients (including EGFR-mutant NSCLC and EGFR-wild type NSCLC) as part of SKB264's global phase 1/2 trial. In China, we completed patient enrollment for the HR+/HER2- BC cohort of SKB264's global phase 1/2 trial in selected advanced solid tumors and expect to advance to phase 3 in the second half of 2023. Notably, SKB264 was also granted Breakthrough Therapy Designation by the NMPA in January 2023 based on the encouraging efficacy and well-tolerated safety data for the treatment of EGFR-TKI failed advanced NSCLC. This designation indicates the promising potential of SKB264 for satisfying the medical needs of patients who have failed EGFR-TKI therapy, by providing a new treatment option besides chemotherapy, which remains the later-line standard treatment but has limited efficacy. We expect to commence a phase 3 trial in the second half of 2023 in EGFR-mutant NSCLC patients who have failed EGFR-TKI therapy.

Further, we are actively exploring the potential of SKB264 for treating other major indications, including advanced GC, OC and other tumor types, for which no TROP2 ADCs were approved globally as of the Latest Practicable Date and where we may have a potential fast- or first-to-market advantage. We are enrolling more patients in the dose expansion cohorts in SKB264's global phase 1/2 trial.

Earlier Treatment Line Expansion via Combination Therapies with Our Backbone Immunotherapy Asset. SKB264-mediated tumor cell killing may synergize with immunotherapies such as PD-(L)1 inhibitors by drawing more T cells to the tumor site and enhancing anti-tumor immunity. To explore this potential synergy, we are evaluating the combination potential of SKB264 with our lead immunotherapy candidate, A167 (PD-L1 mAb), in the front-line setting for various prevalent and hard-to-treat tumor types, starting with advanced EGFR-wild type and EGFR-mutant NSCLC (with or without chemotherapy) and advanced TNBC. We initiated a phase 2 trial to evaluate SKB264 plus A167 with or without chemotherapy as an early-line treatment for advanced EGFR-wild type and EGFR-mutant NSCLC in May 2022 and a phase 2 trial to evaluate SKB264 with or without A167 as a first-line treatment for advanced TNBC in July 2022.

Collaborating with MSD to Advance a Multi-Strategy Clinical Development Plan. We are collaborating with MSD on SKB264's global phase 1/2 trial, as well as two phase 2 basket studies: (i) SKB264 in combination with Keytruda for selected solid tumors, including recurrent or metastatic CC, advanced UC, recurrent OC and metastatic prostate cancer, which we commenced in December 2022 in both China and the U.S. following IND approvals from the NMPA and FDA in July 2022 and November 2022, respectively, and (ii) SKB264 as combination therapies (including with Keytruda, osimertinib and chemotherapy) for advanced EGFR-wild type and EGFR-mutant NSCLC, for which we commenced in China in March 2023 and submitted an IND application to the FDA in January 2023. For details, see "– Our License and Collaboration Arrangements – License and Collaboration Agreement with MSD for SKB264."

The table below sets forth our clinical development plan for SKB264:

Indication (Lines of Treatment)	Trial phase	Mono-/ Combo-therapy	Trial status	(Expected) Trial start date	Location	Hospital sites[1]	Principal investigator(s)[1]	Expected trial end date
Advanced TNBC (3L+)	Phase 3	Mono	Ongoing	April 2022	China	56	Xu Binghe, MD, Yin Yongmei, MD	2H 2025
EGFR-mutant NSCLC (TKI failure)	Phase 3	Mono	CDE consultation completed	(2H 2023)	China	N/A	Zhang Li, MD	2H 2026
TNBC (1L)	Phase 2	Combo with or without A167	Ongoing	July 2022	China	23	Yin Yongmei, MD, Ouyang Quchang, MD	1H 2025
Advanced EGFR-wild type (1L) and EGFR-mutant NSCLC (TKI failure)	Phase 2	Combo with A167 with or without platinum-based chemo	Ongoing	May 2022	China	21	Zhang Li, MD	2H 2024

Indication (Lines of Treatment)	Trial phase	Mono-/ Combo-therapy	Trial status	(Expected) Trial start date	Location	Hospital sites[1]	Principal investigator(s)[1]	Expected trial end date
Advanced EGFR-wild type (1L), EGFR-mutant (TKI failure) and EGFR-mutant (1L) NSCLC	Phase 2	Combo with Keytruda, osimertinib and chemo	China: Ongoing	China: Mar 2023	China[4]	2	Zhang Li, MD	2H 2025
EGFR-mutant NSCLC (2/3L)	Phase 2	Mono	Ongoing	Dec 2022	China	19	Zhang Li, MD	1H 2025
NPC (PD-(L)1 relapsed or refractory)								
Advanced solid tumors[2]	Phase 1/2	Mono	Completed: dose escalation Ongoing: dose expansion	China: Jun 2020 U.S.: Nov 2019	China, U.S.	70 (China), 10 (U.S.)	Li Jin, MD, Jordi Rodon Ahnert, MD, PhD	China and U.S.: 2H 2025
Advanced solid tumors[3]	Phase 2	Combo with Keytruda	China and U.S.: Ongoing	China and U.S.: Dec 2022	Global	11 (China), 4 (U.S.), 1 (Australia)	Wu Xiaohua, MD, Ye Dingwei, MD, Wang Jing, MD	China: 2H 2025 U.S.: 2H 2026

Notes:

(1) Based on public information on ClinicalTrials.gov and ChinaDrugTrials.org.cn.

(2) Including TNBC, HR+/HER2- BC, NSCLC (including EGFR-wild type NSCLC and EGFR-mutant NSCLC), GC, OC, SCLC, UC, HNSCC and EC.

(3) Including recurrent or metastatic CC (2/3L), advanced UC (1L), recurrent and metastatic OC (2L maintenance), and advanced CRPC (2L+).

(4) As of the Latest Practicable Date.

Summary of Clinical Trial Data

We were conducting seven clinical trials for SKB264 as of the Latest Practicable Date. In China and the U.S., we have initiated a phase 1/2 first-in-human clinical trial for selected advanced solid tumors, with dose escalation completed and dose expansion ongoing. Preliminary data from our phase 1/2 clinical trial, including our ongoing dose expansion study, have supported our further clinical trials. We are conducting a pivotal phase 3 clinical trial for advanced TNBC in China upon receiving no material objection from the NMPA. We have also consulted with the CDE regarding a phase 3 clinical trial in EGFR-mutant NSCLC patients who have failed EGFR-TKI therapy, which we plan to initiate in the second half of 2023. In addition to monotherapy trials, we have initiated four clinical trials to investigate SKB264 as part of combination therapies, including two combination trials of SKB264 with A167 in China for advanced NSCLC and advanced TNBC, respectively and a phase 2 basket study of SKB264 as combination therapies (including with Keytruda, osimertinib and chemotherapy) for advanced EGFR-wild type and EGFR-mutant NSCLC in China. Set forth below is a summary of the key data from SKB264's clinical trials.

Pivotal Phase 3 Clinical Trial for Advanced TNBC

This is a randomized registrational trial of SKB264 in patients with locally advanced unresectable, recurrent or metastatic TNBC who have failed 2L+ prior standard of care. This trial plans to enroll 254 adult subjects across about 50 clinical research centers in China.

Trial Objectives. The primary endpoint is the PFS assessed by an independent review committee (IRC) based on response evaluation criteria in solid tumors guideline version 1.1 (RECIST 1.1). The secondary endpoints are the PFS assessed by trial investigators, ORR, DCR (disease control rate), duration of response (DOR), time to objective response (TTR) assessed by the IRC and trial investigators according to RECIST 1.1, overall survival (OS) and quality of life of patients evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire.

Trial Progress. As of the data cut-off date (September 30, 2022), the trial was ongoing, with first-patient-in achieved in August 2022 and 39 patients enrolled in both the experiment group and control group.

Trial Design. Patients are randomized 1:1 into the experiment group and control group, stratified by the number of previous treatment lines (2-3 vs > 3) and presence of liver metastases (yes vs no). The experiment group receives 5 mg/kg of SKB264 via intravenous (IV) injection on day 1 and day 15 of each 28-day cycle. The control group receives one of the following chemotherapy drugs via IV injection: eribulin, gemcitabine, vinorelbine, or capecitabine. Treatment cycle will continue until no more clinical benefits, intolerable toxicity, or patient requesting to discontinue study treatment.

Phase 2 Clinical Trial for Advanced NSCLC with A167 with or without Platinum-based Chemotherapy

This is an open-label, multi-center trial to assess the safety, tolerability profile and the preliminary anti-tumor activity of SKB264 in combination with A167 with or without platinum-based chemotherapy in patients with advanced or metastatic NSCLC. This trial plans to enroll no more than 110 adult subjects across about 20 clinical research centers in China.

Trial Objectives. The primary endpoints are the incidence and severity of AEs, and ORR as assessed by the investigator according to RECIST v1.1 of SKB264 in combination with A167 with or without chemotherapy in patients with advanced or metastatic NSCLC. The secondary endpoints are PFS, DOR, DCR assessed by the investigator according to RECIST v1.1, OS, PK and immunogenicity. The exploratory endpoint is to assess the correlation between anti-tumor activity and the expression level of TROP2 and PD-L1 in tumor tissue.

Trial Progress. As of the data cut-off date (November 29, 2022), this trial was ongoing, with 31 patients with first-line EGFR-wild type advanced NSCLC enrolled and treated with SKB264 5 mg/kg and A167 1200 mg administered every three weeks (Q3W).

Trial Design. This trial comprises three treatment cohorts. Eligible patients with EGFR-wild type or EGFR-mutant NSCLC are assigned to different cohorts to receive SKB264 5 mg/kg Q3W and KL-A167 1200 mg Q3W with or without platinum-based chemotherapy (carboplatin AUC 5 mg/ml/min or cisplatin 75 mg/m^2, Q3W). This trial consists of two parts: the safety run-in period and the expansion period. The safety run-in is conducted in six patients to determine the safety and tolerability of SKB264 in combination with A167 with or without chemotherapy. Once the tolerability of the study treatment is confirmed by the Scientific Review Committee (SRC), subsequent enrollment in expansion period can be continued.

Phase 2 Clinical Trial for Advanced TNBC with or without A167

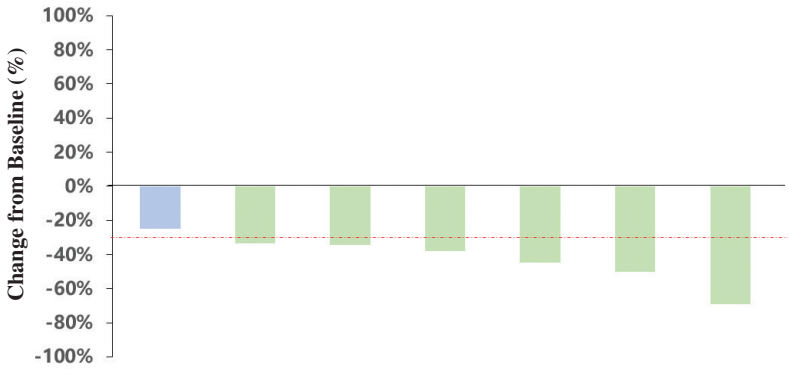
This is a multi-center, open-label trial to assess the safety, tolerability profile, and the preliminary anti-tumor activity of SKB264 monotherapy or in combination with A167 in patients with advanced or metastatic TNBC who have received no prior systemic therapy. This trial plans to enroll no more than 95 adult subjects across about 17 clinical research centers in China.

Trial Objectives. The primary endpoints are the incidence and severity of AEs, and ORR as assessed by the investigator according to RECIST v1.1 of SKB264 monotherapy or in combination with A167 as first-line treatment in patients with advanced or metastatic TNBC. The secondary endpoints are PFS, DOR, DCR assessed by the investigator according to RECIST v1.1, OS, PK and immunogenicity. The exploratory endpoint is to assess the correlation between anti-tumor activity and the expression level of TROP2 and PD-L1 in tumor tissue.

Trial Progress. As of December 6, 2022, this trial was ongoing, with first-patient-in achieved in September 2022 and eight patients with first-line advanced or metastatic TNBC treated with SKB264 5 mg/kg and A167 900 mg Q2W, with four patients on treatment for more than eight weeks.

Trial Design. This trial comprises two treatment cohorts: cohort A is SKB264 5 mg/kg Q2W in combination with A167 900 mg Q2W and cohort B is SKB264 monotherapy. This trial is divided into two parts, part 1 is to explore the safety and the preliminary efficacy of SKB264 in combination with KL-A167. In part 2, patients are randomly divided into the combination group and monotherapy group in a 1:1 ratio.

Efficacy Data. As of the data cut-off date (December 29, 2022), there were seven response-evaluable patients with first-line advanced or metastatic TNBC administered with SKB264 in combination with A167. Of seven response-evaluable patients, six patients achieved PR and one patient had SD with target lesion shrinkage of 25% at first scan. The ORR was 85.7% (including unconfirmed response) and DCR was 100%. The waterfall plot below shows the best percentage change from baseline in target lesions for each evaluable patient.



Safety Data. As of data cut-off date (December 6, 2022), SKB264 in combination with A167 was generally safe and well-tolerated among the eight patients enrolled who received at least one dose of SKB264 in combination with A167. Eight patients (100%) had at least one TRAE related to SKB264 at any grade. Three patients (37.5%) experienced grade 3 or above TRAE. No patient experienced SKB264 or A167-related SAE. TRAEs related to SKB264 are summarized in the table below.

Preferred term	**SKB264 5mg/kg +KL-A167 900mg Q2W (N=8)**	
	All grades (n, %)	**≥ Grade 3 (n, %)**
Any TRAE	8 (100)	3 (37.5)
TRSAE	0	0
Neutropenia	5 (62.5)	1 (12.5)
Lymphopenia	5 (62.5)	0
Anemia	3 (37.5)	0
Thrombocytopenia	3 (37.5)	1 (12.5)
Rash	5 (62.5)	0
Stomatitis	5 (62.5)	0
Alopecia	4 (50)	0
Vomiting	2 (25)	0
Weakness	2 (25)	1 (12.5)

Conclusion. The combination therapy of SKB264 with A167 showed a potentially favorable safety profile and its efficacy results demonstrated promising anti-tumor activity as first-line treatment in patients with advanced or metastatic TNBC.

Phase 1/2 First-in-human Clinical Trial for Selected Advanced Solid Tumors

This is an open-label, multi-center, single-arm, first-in-human clinical trial of SKB264. This trial consists of two parts: dose escalation study in patients with advanced solid tumors and dose expansion study in patients with selected advanced tumor types. Dose escalation was conducted in 30 patients across two clinical research centers in China and eight clinical research centers in the U.S. We plan to enroll 430 patients for dose expansion across 36 clinical research centers in China and nine clinical research centers in the U.S.

Trial Objectives. For the dose escalation study, the primary endpoints were the maximum tolerated dose (MTD) and recommended doses for expansion (RDEs) of SKB264. The secondary endpoints were the overall safety and tolerability profile, ORR, DOR, PFS, OS, the level of anti-drug antibodies (ADA), i.e., the incidence of ADA formation to SKB264, levels of TROP2 expression in tumor tissue, and PK of SKB264. For the dose expansion study, the primary endpoint is ORR. The secondary endpoints include the levels of ADA, levels of TROP2 expression in tumor tissue, PK profile, RDEs, DOR, PFS, and OS of SKB264.

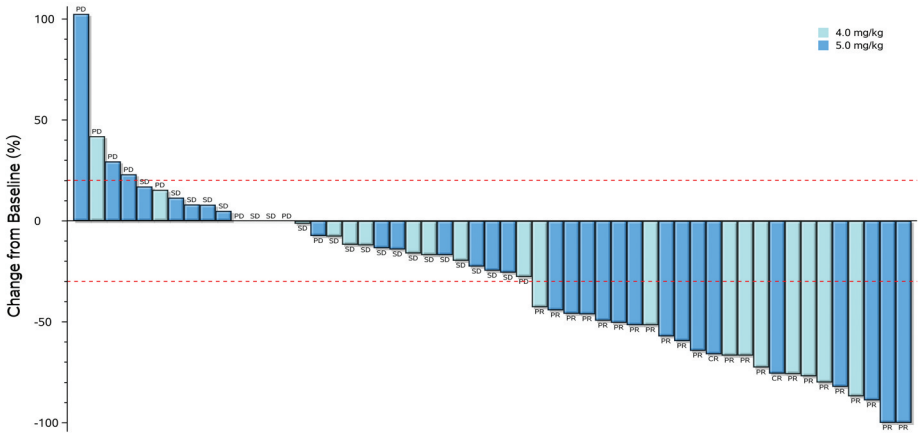
Trial Progress. Dose escalation was completed in December 2021, with 30 patients enrolled and dosed at 2 mg/kg (n=4), 4 mg/kg (n=7), 5 mg/kg (n=7), 5.5 mg/kg (n=5) and 6 mg/kg (n=7). As of December 29, 2022, patient enrollment for the dose expansion cohort was ongoing, with 226 patients enrolled and dosed at 4 mg/kg or 5 mg/kg Q2W.

Trial Design. A Bayesian logistic regression model (BLRM) was adopted in the dose escalation study. Five dose levels were selected for evaluation in the dose escalation study of the trial: 2, 4, 5, 5.5 and 6 mg/kg. Two doses will be given on day 1 and day 15, respectively, for each 28-day cycle of SKB264 treatment. The BLRM evaluated the toxicity of all planned dose levels and some intermediate dose levels. RDEs were selected for the dose expansion cohort based on the safety, efficacy and PK data in dose escalation. Once a dose level was proved to be tolerated with potential clinical benefits in dose escalation, it would be considered as one of the RDEs.

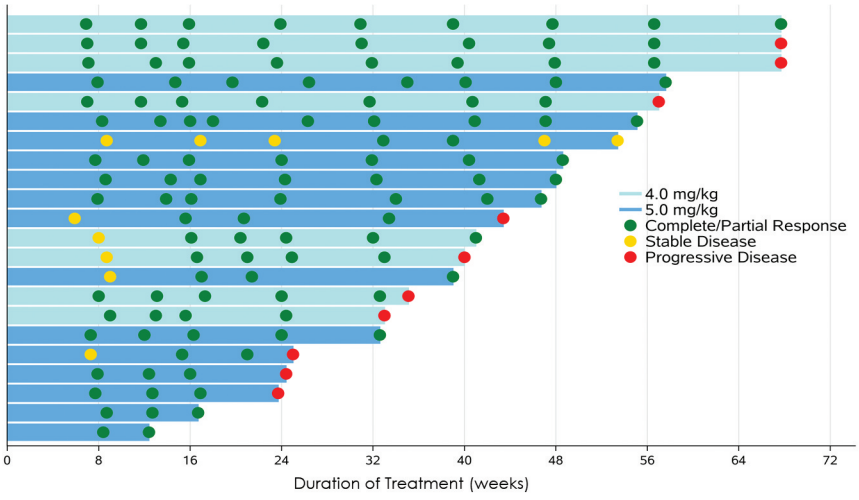
Efficacy Data.

Advanced TNBC. Our advanced TNBC data was presented in the 2022 San Antonio Breast Cancer Symposium (SABCS), one of the world's largest scientific conferences dedicated to breast oncology advancements. As of the data cut-off date (October 10, 2022), 59 patients were enrolled (23 in 4 mg/kg Q2W, 36 in 5 mg/kg Q2W), 88% of patients had received $\geq$ 3 prior therapies for metastatic disease. The median follow-up was 12.8 months.

Of 55 patients (21 in 4 mg/kg and 34 in 5 mg/kg) evaluable for response assessment (defined as a patient with at least one post-baseline tumor assessment), the ORR was 43.6% (24/55), and DCR was 80% (44/55). The median duration of response (DoR) was 11.5 months and the 6-month DoR rate was 77.5%. The median PFS was 5.7 months. Preliminary OS data were encouraging and 12-month OS rate was 66.4%. Among the 53 patients who had tumor response and tissue available for TROP2 testing, 29 patients (55%) had high TROP2 expression (H-score >200-300). The confirmed ORR (cORR), i.e., a PR/CR maintained through a subsequent efficacy assessment at least 28 days later, was 55.2% (16/29) in the subset of patients with high TROP2 expression. The below waterfall plot shows the best percentage change from baseline in target lesions for each evaluable patient.



The swimmer plot below shows the durable objective responses and disease stabilization of the patients who achieved confirmed partial response (PR) or complete response (CR).



HR+/HER2- BC. As of the data cut-off date (Nov 15, 2022), 39 patients were enrolled and treated with SKB264. Of 28 patients evaluable for response assessment, the ORR was 42.9% (12/28, 2 pending confirmation) and DCR was 85.7% (24/28).

NSCLC. As of the data cut-off date (February 9, 2023), 43 patients were enrolled (all in 5 mg/kg, Q2W), with a median follow-up of 11.5 months. Of 39 patients evaluable for response assessment, the ORR was 43.6% (17/39, 2 pending confirmation), DCR was 94.9% (37/39), median DoR was 9.3 months and the 6-month DoR rate was 76.9%. For EGFR wild-type subgroup (previously received median 2 lines of therapy including anti-PD-(L)1 therapy), the ORR was 26.3%, DCR was 89.5% (17/19), median PFS was 5.3 months and 9-month OS rate was 80.4%. For the subgroup with TKI-resistant EGFR-mutant NSCLC (among which 50% also failed at least one line of chemotherapy), the ORR was 60.0% (12/20), DCR was 100% (20/20), median PFS was 11.1 months and 9-month PFS rate was 66.7%.

Safety Data. SKB264 was safe and well-tolerated in the completed dose escalation study. TRAEs were reported in 28 (93.9%) patients enrolled in the dose escalation study. 17 (56.7%) patients experienced grade 3 or above TRAEs, with the most frequent ones (incidence ≥ 5%) being anemia (26.7%), neutropenia (23.3%), leukopenia (16.7%), stomatitis (16.7%) and thrombocytopenia (13.3%). Patients recovered from all TRAEs of grade 3 or above after corresponding treatment. There were no TRAEs that resulted in death.

As of the data cut-off date (August 21, 2022), 211 patients had received at least one dose of SKB264 in the dose expansion study. 23 and 188 patients with different types of advanced solid tumors were treated with SKB264 at the dose level of 4 mg/kg Q2W and 5 mg/kg Q2W, respectively. Treatment-related adverse events (TRAEs) were reported in 202 (95.7%) patients. TRAEs of grade 1 or 2 occurred in 101 (47.9%) patients and were recovered with supportive care or after dose modification. Grade 3 or above TRAEs were reported in 110 (52.1%) patients. Treatment-related serious adverse events (TRSAEs) occurred in 51 (24.2%) patients. No TRAEs leading to death was reported. The safety profile of SKB264 monotherapy was tolerable and manageable. TRAEs at the dose level of 4 mg/kg Q2W and 5 mg/kg Q2W are summarized in the table below.

TRAEs at the dose of 4 mg/kg Q2W and 5 mg/kg Q2W[(1)]

Preferred term	**SKB264 4 mg/kg Q2W (N=23)**		**SKB264 5 mg/kg Q2W (N=188)**	
	All grades	**≥ Grade 3**	**All grades**	**≥ Grade 3**
	(n, %)	**(n, %)**	**(n, %)**	**(n, %)**
Any TRAE	23 (100)	11 (47.8)	179 (95.2)	99 (52.7)
Anemia	17 (73.9)	4 (17.4)	136 (72.3)	44 (23.4)
Leukopenia	17 (73.9)	3 (13.0)	113 (60.1)	32 (17.0)
Neutropenia	14 (60.9)	2 (8.7)	106 (56.4)	49 (26.1)
Nausea	10 (43.5)	0	58 (30.9)	2 (1.1)
Vomiting	10 (43.5)	0	50 (26.6)	1 (0.5)
Stomatitis	6 (26.1)	1 (4.3)	82 (43.6)	16 (8.5)
Alopecia	3 (13.0)	0	60 (31.9)	0 (0.0)
Rash	6 (26.1)	0	66 (35.1)	8 (4.3)
Thrombocytopenia	6 (26.1)	3 (13.0)	65 (34.6)	15 (8.0)

Note:

(1) Data cut-off as of August 21, 2022. All grade TRAEs occurred in ≥ 20% of patients or ≥ Grade 3 TRAEs occurred in > 1 subjects.

PK Data. In PK analysis in the dose escalation study, the exposure of SKB264 increased proportionally with dose within the tested dose range of 2 to 6 mg/kg. No accumulation of SKB264 was observed after multiple doses. The half-lives of SKB264 and free payload were approximately 36 hours and 49 hours, respectively, supporting a once every two weeks dosing regimen. The plasma exposure of the free payload, indicated by maximum plasma

concentration (C_{max}) and area under the curve (AUC), were approximately 6% and 5%, respectively, as those of SKB264 in the first 4-week cycle, while the PK parameters and plasma exposure of the total antibody, which refers to conjugated, partially unconjugated and fully unconjugated antibodies, were similar to those of SKB264. These results suggested that the linker of SKB264 was stable during systemic circulation and most payload molecules were directed by the targeted antibody to the tumor tissue.

Conclusion. SKB264 monotherapy exhibited a potentially favorable safety profile in patients with advanced solid tumors and its preliminary efficacy results demonstrated encouraging anti-tumor activities across a range of tumor types.

Material Communications and Next Steps

We received IND approvals from the NMPA in April 2020 and the FDA in August 2019 for the initiation of SKB264's global phase 1/2 trial for advanced solid tumors. We completed the phase 1 dose escalation part of the global phase 1/2 trial in December 2021. Taking into the industry practice as advised by Frost & Sullivan and as advised by PRC Legal Advisers with respect to PRC laws and regulations, the phase 1 dose escalation study was a completed clinical trial with its main purpose aligning with the overall purpose of a conventional phase 1 trial, and therefore the completion of the phase 1 dose escalation study is equivalent to the completion of a conventional phase 1 trial. We completed consultation with the CDE in April 2022 on our preliminary phase 1/2 results and the trial design of our pivotal phase 3 trial for advanced TNBC. The CDE expressed no major concerns on the preliminary results of our phase 1/2 clinical trial and no objection to the commencement of this pivotal phase 3 trial for advanced TNBC.

The NMPA granted Breakthrough Therapy Designation to SKB264 for advanced TNBC in July 2022 and for EGFR-TKI failed EGFR-mutant advanced NSCLC in January 2023. We commenced our pivotal phase 3 trial for advanced TNBC in China in April 2022 and expect to complete patient enrollment in the second half of 2023.

For SKB264 combination therapies, we obtained IND approvals from the NMPA in March and April 2022 for two phase 2 clinical trials – a phase 2 trial of SKB264 in combination with A167 with or without chemotherapy, as an early-line treatment for advanced EGFR-wild type and EGFR-mutant NSCLC and a phase 2 trial of SKB264 with or without A167 as a first-line treatment for advanced TNBC. Further, we received IND approvals from the NMPA and FDA in July 2022 and November 2022, respectively, for a global phase 2 basket study of SKB264 in combination with Keytruda for selected solid tumors, which we commenced in December 2022 in China. For SKB264's phase 2 basket study as combination therapies (including with Keytruda, osimertinib and chemotherapy) for advanced EGFR wild-type and EGFR-mutant NSCLC, we commenced the trial in March 2023 in China after receiving IND approval from the NMPA in January 2023. We also submitted an IND application to the FDA for this basket study in January 2023.

The table below sets forth the timeline of preclinical studies and clinical trials for SKB264.

Milestone/Stage	Timeline	Hospital sites	Principal investigator(s)
Preclinical development (PCC to IND-enabling stage)	March 2018 – July 2019	N/A	N/A
IND approval	U.S.: August 2019	N/A	N/A
Phase 1/2 trial for selected advanced solid tumors	China: April 2020 *Dose escalation* U.S.: November 2019 – December 2021 China: June 2020 – December 2021 *Dose expansion* U.S.: November 2019 – ongoing China: June 2020 – ongoing	70 (China), 10 (U.S.)	Li Jin, MD, Jordi Rodon Ahnert, MD, PhD
Pivotal phase 3 trial for advanced TNBC	April 2022 – ongoing	56	Xu Binghe, MD, Yin Yongmei, MD
Phase 2 trial for advanced NSCLC with A167 with or without platinum-based chemotherapy	May 2022 – ongoing	21	Zhang Li, MD
Phase 2 trial for advanced TNBC with or without A167	July 2022 – ongoing	23	Yin Yongmei, MD, Ouyang Quchang, MD
Phase 2 basket study for advanced EGFR-wild type and EGFR-mutant NSCLC with Keytruda, Osimertinib and chemotherapy	China: March 2023 – ongoing U.S.: IND submitted	2 (China)	Zhang Li, MD
Phase 2 trial for EGFR-mutant NSCLC and NPC	December 2022 – ongoing	19	Zhang Li, MD
Phase 2 basket study for advanced solid tumors with Keytruda	U.S. and China: December 2022 – ongoing	11 (China), 4 (U.S.), 1 (Australia)	Wu Xiaohua, MD, Ye Dingwei, MD, Wang Jing, MD

As of the Latest Practicable Date, we had received no major concerns or objections from the NMPA or FDA to our clinical development plan for SKB264.

SKB264 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

A166 – A Differentiated HER2 ADC, Our Core Product

Overview

A166 is a differentiated, internally discovered and developed HER2 ADC in NDA registration stage for treating advanced HER2+ solid tumors. It is positioned to target multiple cancer indications with high prevalence and medical needs, with the potential to be one of the first domestically developed ADCs for advanced HER2+ BC in China. HER2 overexpression is a well-established oncogenic driver across a wide range of cancers, including prevalent cancer types, such as BC and GI cancers (GC and CRC). Although three HER2 ADCs, Kadcyla, Aidixi and Enhertu, have been approved in China, their therapeutic efficacy is limited to a minority of HER2+ solid tumor patients, leaving a significant unmet need for differentiated HER2 ADCs to widen the treatment options available for advanced HER2+ solid tumor patients.

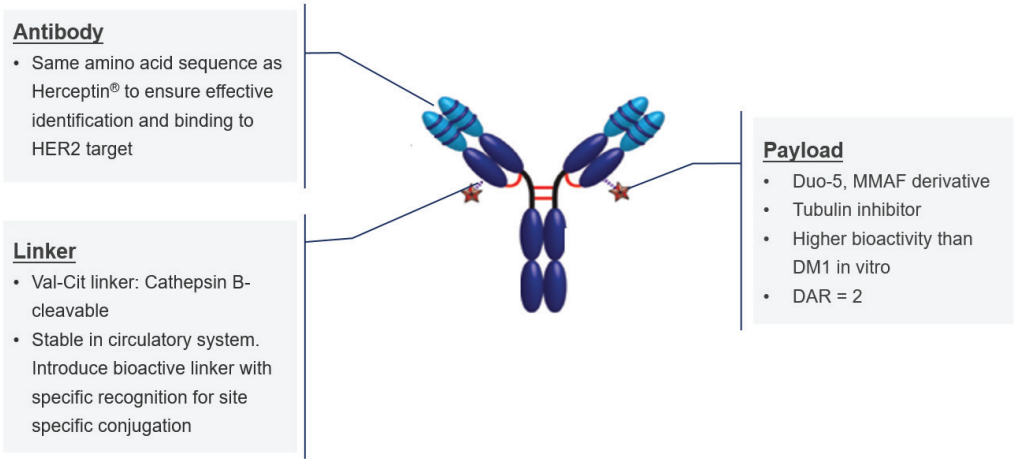
Configured with a potent cytotoxic payload, clinically proven mAb and site-specific conjugation technology, A166 demonstrated promising efficacy in heavily pre-treated advanced HER2+ BC patients with an ORR of 73.9% at RP2D and in advanced HER2+ GC patients with an ORR of 31.3% , based on preliminary results from our ongoing phase 1 dose expansion study and ongoing phase 1b trial in China. A166 also showed a differentiated safety profile from that of Kadcyla, Enhertu and Aidixi, the only three NMPA and/or FDA-approved HER2 ADCs as of the Latest Practicable Date, with lower incidence of haematological, GI and lung toxicities in non-head-to-head, cross-trial comparisons. Although A166 demonstrated higher incidences of ocular and peripheral nerve-related toxicities, they were reversible and generally manageable. This suggests the potential of A166 to widen the treatment options available to advanced HER2+ solid tumor patients with different susceptibility to adverse drug reactions.

We have designed a multi-indication clinical development plan to advance A166 in China. In May 2023, we submitted an NDA to the NMPA for A166 as a 3L+ treatment for patients with advanced HER2+ BC. We completed the dose escalation study of a phase 1 trial for advanced HER2+ solid tumors with the dose expansion study anticipated to be concluded in the second half of 2024. We are conducting a pivotal phase 2 trial for advanced HER2+ BC, in which A166 has met the primary endpoints based on results from the primary analysis, which we used to submit an NDA to the NMPA in May 2023. In addition to advanced HER2+ BC, we are exploring the therapeutic potential of A166 for other advanced HER2+ solid tumors, including GC and CRC, in ongoing phase 1b clinical trials.

Drug Design and Mechanism of Action

HER2 is a cell surface receptor expressed at low levels in various tissues such as the breast, lungs, and GI tract, where it promotes cell growth and survival. In tumor cells, mutations or amplification in the HER2 gene may result in the overexpression of HER2, i.e., excessive copies of the HER2 protein, which drives uncontrollable cell growth that promotes cancer development.

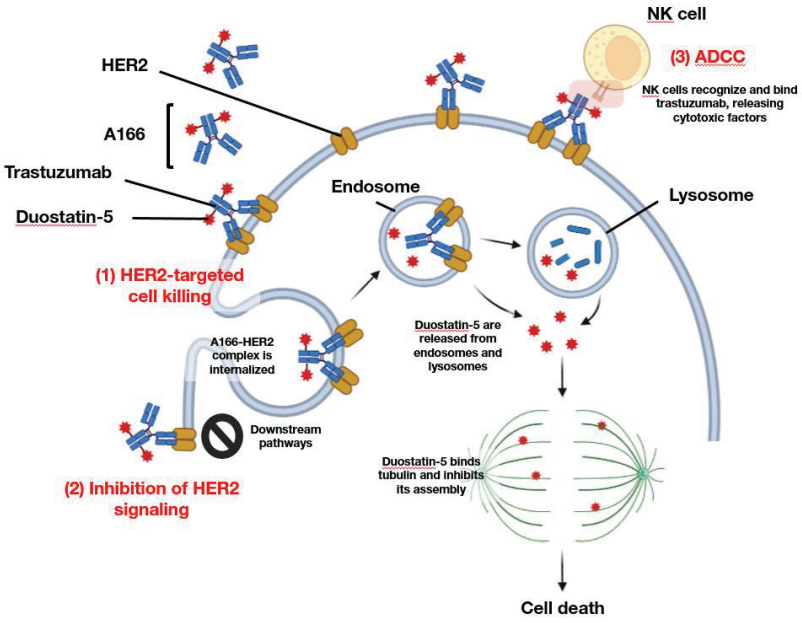
A166 is developed with the following core components and features to optimize safety and efficacy.



Abbreviations: Duo-5: duostatin-5; MMAF: monomethyl auristatin F; Val-Cit: valine-citrulline; DM1: emtansine

It employs a high payload toxicity-low DAR design, in which a novel, highly cytotoxic tubulin inhibitor, duostatin-5, is conjugated at a low DAR via a stable, enzyme-cleavable linker to a HER2 mAb, which has the same amino acid sequence as Herceptin (trastuzumab), a clinically proven HER2 mAb, to ensure effective identification of and binding to HER2. We use site-specific conjugation technology to generate ADCs with a homogeneous DAR.

As illustrated in the diagram below, the design of A166 potentially enables strong anti-tumor activity via HER2-targeted cell killing, inhibition of HER2 signalling and antibody-dependent cellular cytotoxicity (ADCC). Following its binding to the HER2 receptor via trastuzumab, the A166-HER2 complex is internalized and transported via the endosome-lysosome pathway, which is a system of membrane-enclosed compartments where degradative enzymes cleave the valine-citrulline linker. This releases duostatin-5, which then binds to and inhibits the assembly of tubulin, a major protein required for the maintenance of cellular architecture, thereby interfering with the cell division cycle and triggering apoptosis that kills the tumor cells. Moreover, trastuzumab, the mAb component of A166, can block HER2 from propagating oncogenic signals to downstream signalling molecules, thereby inhibiting the major signalling route that HER2+ tumor cells rely on for growth and expansion. Further, trastuzumab can trigger ADCC, an immune-mediated attack, in which trastuzumab is recognized and bound by natural killer (NK) cells, which can release cytotoxic factors that kill the A166-bound tumor cells.



Market Opportunity and Competition

We are developing A166 in China to treat patients with advanced HER2+ solid tumors, including HER2+ BC, HER2+ GC and HER2+ CRC. The China market of HER2 ADCs is expected to increase from RMB0.6 billion in 2022 to RMB8.4 billion by 2030, representing a CAGR of 38.2%. For more details regarding the competitive landscape of HER2 ADCs in China, see "Industry Overview – China's HER2 ADC Market – Competitive Landscape of HER2 ADCs."

The following table summarizes the major indications targeted by A166.

Disease indication	Sub-type	Treatment paradigm	Positioning of A166[1]
BC	HER2+ BC	First-line: combination chemo with trastuzumab and pertuzumab, doublet chemo with trastuzumab	3L+
		Later-line: combination chemotherapy with TKI or HER2 mAb, HER2 ADC (Kadcyla)	
GC	HER2+ GC	First-line: combination chemo with trastuzumab, PD-1 inhibitor (PD-L1-positive only)	2L+
		Later-line: combination chemo with trastuzumab, single-agent chemo, other chemo regimens, PD-1 inhibitor, Aidixi (China-only), apatinib	

Disease indication	Sub-type	Treatment paradigm	Positioning of A166[1]
CRC	HER2+ CRC	First-line: PD-1 inhibitor, FOLFOX or FOLFIRI with or without cetuximab or bevacizumab, CAPEOX, chemo with or without bevacizumab	3L+
		Later-line: FOLFOX/FOLFIRI with or without cetuximab or bevacizumab, CAPEOX with or without bevacizumab	

Note:

(1) In the China market.

HER2+ BC. HER2+ BC is a major subtype of BC and accounts for approximately 15-30% of total BC cases. Compared to HER2– BC, HER2+ BC is associated with more aggressive, fast-growing tumors and a worse prognosis. About 20-25% of all patients with HER2+ BC have advanced disease at diagnosis, and about 20% of early-stage patients eventually develop advanced disease. According to Frost & Sullivan, the incidence of HER2+ BC in China increased from 80.1 thousand in 2017 to 86.6 thousand in 2022 and is expected to reach 94.1 thousand in 2030.

The treatment paradigm for advanced HER2+ BC patients eligible for HER2 mAb trastuzumab in China primarily involves combination chemotherapy with two HER2 mAbs, trastuzumab and pertuzumab, or doublet chemotherapy with trastuzumab in the first-line setting, combination chemotherapy with TKI pyrotinib or HER2 mAb in the 2L setting, and triple-combination therapy involving a HER2 mAb pertuzumab or TKIs, and other chemotherapy in the 3L setting. For advanced HER2+ BC patients not eligible for trastuzumab, the treatment paradigm in China primarily involves combination chemotherapy with TKI pyrotinib in the first-line setting, HER2 ADC Kadcyla monotherapy and combination chemotherapy with TKI lapatinib in the 2L setting, and combination chemotherapy with TKI neratinib, TKI pyrotinib monotherapy and other TKI/HER2 mAb-chemotherapy combinations in the 3L setting. HER2 ADC Enhertu monotherapy is also approved for patients with unresectable or metastatic HER2+ BC who have received one or more prior anti-HER2-based regimens. Despite the advances in anti-HER2 therapies, a significant number of patients remain unresponsive or experience treatment resistance and/or significant side effects. Kadcyla and Enhertu, for example, carry notable safety concerns, including black box warning issued by the FDA for hepatic, cardiac and embryo-fetal toxicities for Kadcyla, and interstitial lung disease and embryo-fetal toxicity for Enhertu. These limitations highlight a significant unmet need for safer treatments that can prolong the survival for relapsed or refractory patients. As of the Latest Practicable Date, according to Frost & Sullivan, Kadcyla and Enhertu were the only HER2 ADCs approved for advanced HER2+ BC in China, and there were nine HER2 ADCs in China in phase 2 or beyond for treating advanced HER2+ BC. For further details, see "Industry Overview – China's HER2 ADC Market – Competitive Landscape of HER2 ADCs."

HER2+ GC. GC is the sixth most common and the third most deadly cancer worldwide, with China being one of the countries with the highest GC incidence. HER2 overexpression is reported in approximately 10-30% of GC patients, and it represents an important actionable oncogenic alteration in GC. According to Frost & Sullivan, the incidence of HER2+ GC in China increased from 102.5 thousand in 2017 to 119.2 thousand in 2022 and is expected to reach 148.1 thousand in 2030. Approximately 50% of HER2+ GC patients are diagnosed with advanced disease.

In China, the early-line treatments for HER2+ GC primarily involve combination chemotherapy with HER2 mAb trastuzumab and single-agent chemotherapy (in the 2L setting), with HER2 ADC Aidixi, an anti-angiogenic TKI, PD-1 inhibitors and single-agent chemotherapy available as 3L+ treatments. The use of trastuzumab in combination with chemotherapy in early-line HER2+ GC patients generally improves patient outcome compared with conventional chemotherapy. However, a significant portion of patients do not respond to trastuzumab and the majority of patients who initially benefit from trastuzumab develop drug resistance. These patients have limited effective 2L+ treatment options, with Aidixi being the only HER2-directed drug available in the 3L+ setting. This underscores a significant unmet need for novel HER2-directed drugs to overcome trastuzumab resistance and widen the treatment options for 2L+ HER2+ GC patients. As of the Latest Practicable Date, according to Frost & Sullivan, HER2 ADC Aidixi was the only HER2 ADC approved in China for advanced HER2+ GC, and there were ten HER2 ADCs in phase 1 or beyond for HER2+ GC in China. For further details, see "Industry Overview – China's HER2 ADC Market – Competitive Landscape of HER2 ADCs."

HER2+ CRC. CRC is the third most common cancer and one of the leading causes of cancer mortality in China. HER2 is reported to be overexpressed in approximately 3-5% of CRC. According to Frost & Sullivan, the incidence of HER2+ CRC in China increased from 16.5 thousand in 2017 to 19.3 thousand in 2022 and is expected to reach 24.1 thousand in 2030. Approximately 36% of HER2+ CRC patients are diagnosed with advanced disease.

In China, the early-line treatments for HER2+ CRC primarily involve chemotherapy with or without EGFR mAb cetuximab or anti-angiogenic mAb bevacizumab. As of the Latest Practicable Date, there were no HER2-directed drugs approved by the NMPA for advanced HER2+ CRC. The response rates of advanced HER2+ CRC patients to current non-HER2-directed standard treatments are only between 10.0% to 35.3%, leaving many patients with limited clinical benefit and highlighting the significant unmet need for novel HER2-directed drugs to improve the survival of advanced HER2+ CRC patients. As of the Latest Practicable Date, there were two HER2 ADCs in phase 1 or beyond for HER2+ CRC in China. For further details, see "Industry Overview – China's HER2 ADC Market – Competitive Landscape of HER2 ADCs."

Competitive Advantages

Site-specific Low-DAR Conjugation for Highly Potent Payload. A166 is armed with a highly cytotoxic payload that can exert potent tumor cell killing at a low DAR. Coupled with a uniformly low DAR, achieved via our site-specific conjugation technology, this design potentially ensures the safety of A166 by enhancing ADC stability and reducing premature payload release in blood circulation, while maintaining robust anti-tumor potency.

Promising Anti-tumor Effect. Based on preliminary results from our ongoing phase 1 dose expansion study, A166 demonstrated promising efficacy, highlighted by an ORR of 73.9% at RP2D (4.8 mg/kg Q3W). Notably, we specifically enrolled patients whose treatment histories were in line with the current treatment paradigm for advanced HER2+ BC in China to better reflect the intended use population. In addition to its promising preliminary efficacy against advanced HER2+ BC, A166 also showed encouraging efficacy against advanced HER2+ GC with an ORR of 31.3% based on preliminary results from our ongoing phase 1b trial. Although no head-to-head data are available at this stage, we believe the following comparisons with Kadcyla, Enhertu and Aidixi shed light on the differentiated features and advantages of A166 from an efficacy perspective, based on the latest non-head-to-head data publicly available.

		ORR		
Tumor type	**A166 (4.8 mg/kg Q3W)**	**Kadcyla**	**Enhertu**	**Aidixi**
Advanced HER2+ BC[1]	73.9%	43.6%	60.9%	34.4%
Advanced HER2+ GC[2]	31.3%	N/A	40.5%	24.4%

Sources:

(1) Kadcyla: Dieras V, et al. Lancet Oncol 2017; Enhertu: Modi S, et al. New Engl J Med 2020; Aidixi: SABCS19-PD4-06 published in February 2020

(2) Enhertu: Enhertu's drug label: Aidixi: Aidixi's drug label

The promising efficacy demonstrated by A166 indicates its potential as an effective treatment option for advanced HER2+ solid tumor patients in China.

Potentially Differentiated Safety Profile. Supported by its drug design for balanced efficacy and safety, A166 demonstrated high stability in systemic circulation in heavily pre-treated advanced HER2+ BC patients based on preliminary results from its overall phase 1 trial, where it showed a differentiated safety profile from Kadcyla, Enhertu and Aidixi, with lower incidence of haematological, GI and lung toxicities in non-head-to-head cross-trial comparisons. Although A166 demonstrated higher incidences of ocular and peripheral nerve-related toxicities, they were reversible and generally manageable. Although no head-to-head data are available at this stage, we believe the following comparison sheds light on the differentiated features and advantages of A166 from a safety perspective. With a differentiated safety profile, A166 has the potential to widen the treatment options available for advanced HER2+ BC patients with different susceptibility to adverse drug reactions.

Preferred term		Kadcyla (3.6 mg/kg, Q3W, N=490)	Enhertu (5.4 mg/kg, Q3W, N=234)	Aidixi (2.5 mg, Q2W, N=350)	A166 (4.8 and 6.0 mg/kg, Q3W, N=77)
		Adverse drug reaction incidence[1] (%)			
Anemia	Total	14.3	31	22.6	23.4
	≥ Grade 3	4.1	7	2.6	3.9
Decreased platelet count	Total	83	37	16.0	3.9
	≥ Grade 3	17	3.4	1.1	0
Decreased neutrophil count	Total	39	62	50.6	9.1
	≥ Grade 3	3	16	16.9	1.3
Decreased white blood cell count	Total	N/A	70	55.4	20.8
	≥ Grade 3	N/A	7	10.9	4.2
Nausea	Total	39.8	79	31.1	9.1
	≥ Grade 3	0.8	7	0.3	0
Vomiting	Total	19.2	47	18.3	5.2
	≥ Grade 3	0.8	3.8	0.6	0
Diarrhea	Total	24.1	29	11.4	9.1
	≥ Grade 3	1.6	1.7	0.3	0
Elevated aspartate aminotransferase	Total	98	41	49.7	18.2
	≥ Grade 3	<8	0.9	16	0
Elevated alanine aminotransferase	Total	82	38	42.9	18.2
	≥ Grade 3	<6	0.4	1.7	0
Peripheral neuropathy	Total	21.2	N/A	5.1	54.5
	≥ Grade 3	2.2	N/A	1.1	6.5
Corneal disease	Total	3.9	N/A	N/A	94.8
	≥ Grade 3	0	N/A	N/A	36.4
Dry eye	Total	3.9	11.1	N/A	40.3
	≥ Grade 3	0	0.4	N/A	15.6
Blurred vision	Total	4.5	N/A	N/A	85.7
	≥ Grade 3	0	N/A	N/A	24.7
ILD	Total	N/A	9.0	N/A	2.6
	≥ Grade 3	N/A	2.6	N/A	0

Note:

(1) This table summarizes the common drug adverse reactions and laboratory abnormalities (≥10% all grades or ≥2% grades 3 or 4) for A166, Kadcyla, Enhertu, or Aidixi.

Sources:

(1) Kadcyla: Kadcyla's drug label; Enhertu: Enhertu's drug label; Aidixi: Aidixi's drug label

For further details about the efficacy and safety of A166 in the ongoing clinical trials, see "– Our Pipeline – Oncology Franchise – ADCs – A166 – Summary of Clinical Trial Data."

Clinical Development Plan

We are executing a multi-indication clinical development plan for A166 in China to explore the potential of A166 for treating various advanced HER2+ solid tumors. Based on the approval from the NMPA, we are conducting a pivotal phase 2 trial to evaluate the potential of A166 as a 3L+ treatment for advanced HER2+ BC. Upon meeting the primary endpoint in our pivotal phase 2 trial, we have filed an NDA for conditional approval in May 2023, which is under priority review. Although we have completed the study per protocol, the trial is still ongoing as certain patients responsive to the drug continue with treatment. Pending consultation with the CDE, we plan to commence a confirmatory phase 3 trial to explore A166 as a 2L+ treatment for advanced HER2+ BC in the second half of 2023. We are also conducting two phase 1b trials to evaluate A166 for patients with advanced HER2+ GC and advanced HER2+ CRC, respectively, which we expect to conclude in the first half of 2024.

The table below sets forth our clinical development plan for A166:

Indication (Lines of Treatment)	Trial phase	Trial status	(Expected) Trial start date	Hospital sites[(1)]	Principal investigator(s)[(1)]	Expected trial end date
Advanced HER2+ BC (2L+)	Phase 3	CDE clinical consultation	(2H 2023)	N/A	N/A	2H 2025
Advanced HER2+ BC (3L+)	Phase 2	Ongoing	August 2021	39	Hu Xichun, MD	2H 2023
Advanced HER2+ GC (2L+)	Phase 1b	Ongoing	December 2021	20	Liu Tianshu, MD	2H 2023
Advanced HER2+ CRC (3L+)	Phase 1b	Ongoing	December 2021	21	Xu Ruihua, MD	2H 2023
Advanced HER2+ solid tumors	Phase 1	Completed: dose escalation Ongoing: dose expansion	August 2018	3	Hu Xichun, MD	1H 2024

Note:

(1) Based on public information on ClinicalTrials.gov and ChinaDrugTrials.org.cn

Summary of Clinical Trial Data

Set forth below is a summary of the key data from A166's completed and ongoing clinical trials.

Pivotal Phase 2 Clinical Trial for Advanced HER2+ BC

This is an open-label, multi-center, single-arm pivotal trial to evaluate the efficacy of A166 in Chinese patients with locally advanced unresectable, relapsed, or metastatic HER2+ BC who have failed 2L+ treatments. This trial is conducted in 123 adult subjects across 39 clinical research centers in China.

Trial Objectives. The primary endpoint is the IRC-assessed ORR based on RECIST 1.1. The secondary endpoints are the ORR assessed by trial investigators, PFS, OS, survival rates, safety, immunogenicity, and PK of A166.

Trial Progress. A166 has met the primary endpoints based on results from the primary analysis, after all enrolled patients had undergone a follow-up period of at least six months. As of the Latest Practicable Date, this trial was ongoing with some patients still responsive to A166 and continuing to receive treatment.

Trial Design. Subjects receive 4.8 mg/kg of A166 injection once every 21 (±3) days until disease progression, intolerable toxicity, death, withdrawal of informed consent, or other treatment termination criteria are met.

Phase 1b Clinical Trial for Advanced HER2+ GC or Esophagogastric Junction Adenocarcinoma

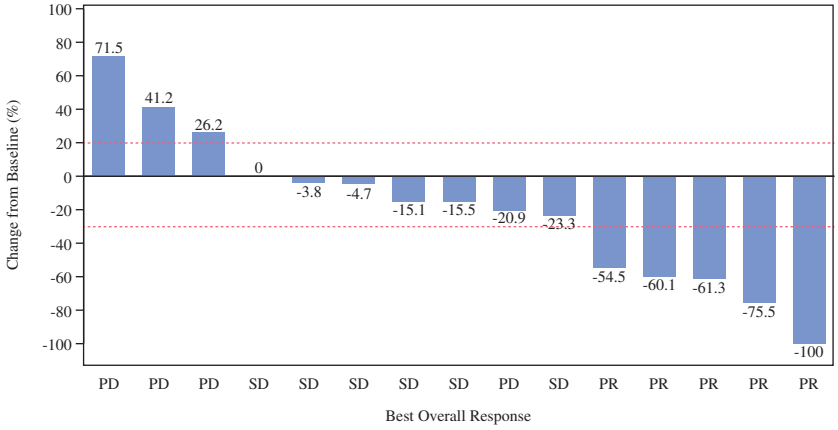
This is an open-label, multi-center, single-arm trial to evaluate the safety, tolerability and efficacy, and to determine the RP2D of A166 in 2L+ patients with locally advanced unresectable or metastatic HER2+ GC or esophagogastric junction adenocarcinoma. This trial is conducted in 16 adult subjects in 11 clinical research centers across China.

Trial Objectives. The primary endpoints include A166's safety, tolerability and ORR. The secondary endpoints include other efficacy parameters including DOR, DCR and PFS, the PK characteristics of A166 and duostatin-5, and the immunogenicity of A166.

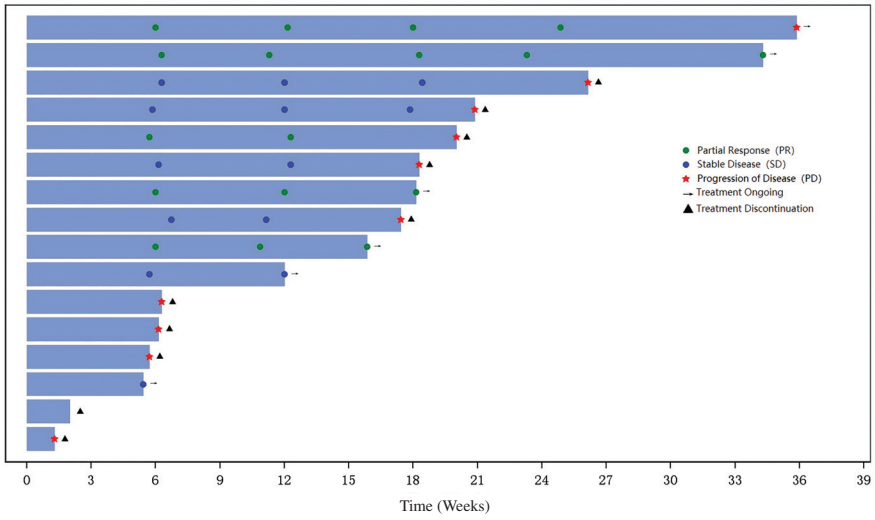
Trial Progress. As of the Latest Practicable Date, this trial was ongoing with patient enrollment completed in December 2022. As of February 9, 2023, 16 patients were enrolled and dosed at 4.8 mg/kg of A166 injection Q3W, with a median follow-up of 6.7 months. As of the same date, five (31.3%) patients were still receiving treatment.

Trial Design. Subjects receive 4.8 mg/kg of A166 injection Q3W until disease progression, intolerable toxicity, or withdrawal of informed consent.

Efficacy Data. As of the data cut-off date (February 9, 2023), of 16 patients evaluable for response assessment, the ORR was 31.3% (5/16), and DCR was 68.8% (11/16). The median PFS was 4.6 months. The below waterfall plot shows the best percentage change from baseline in target lesions for each evaluable patient.



The swimmer plot below shows the responses of 16 evaluable patients to A166 treatment over time.



Safety Data. As of the data cut-off date (February 9, 2023), 93.8% of patients experienced TRAEs, which were mainly ocular-related and were reversible. Most frequent TRAEs in the 16 evaluable patients were blurred vision (68.8%), corneal epitheliopathy (68.8%), dry eye (50.0%), neutropenia (25.0%), lymphopenia (25.0%), anemia (25.0%) and weight loss (25.0%). Grade 3 or higher TRAEs were reported in 37.5% of patients.

Conclusion. A166 was generally safe and well-tolerated in 2L+ advanced HER2+ GC patients with promising anti-tumor efficacy, based on preliminary results.

Phase 1 Clinical Trial for Advanced HER2+ Solid Tumors (KL166-I-01-CTP;CTR20181301)

This is a single-arm, dose-escalation and dose expansion trial to evaluate the safety, tolerability, PK, and anti-tumor activity of A166 in Chinese patients with locally advanced unresectable or metastatic HER2+ solid tumors who progressed on or did not respond to available standard therapies. The dose escalation study was conducted in 25 patients and the dose expansion study plans to enroll 71 patients across three clinical research centers in China.

Trial Objectives. The primary endpoint of the dose escalation study was the maximum tolerated dose (MTD) and recommended stage 2 dose (RS2D) of A166. The secondary endpoints were the dose-limiting toxicity, safety, preliminary efficacy, PK and immunogenicity of A166. The primary endpoint of the dose expansion study was the ORR. The secondary endpoints are the safety, DCR, PFS, OS, and PK of A166.

Trial Progress. The dose escalation study was completed in April 2020. As of the Latest Practicable Date, patient enrollment of the dose expansion study was ongoing, with first-patient-in achieved in May 2020.

Trial Design. This trial consists of two parts, i.e., dose escalation and dose expansion. In the dose escalation study, patients were randomly assigned into eight cohorts to receive escalating doses of A166 from 0.1 to 6.0 mg/kg, administered once every three weeks. In the dose expansion study, patients are randomly assigned to receive A166 at the RS2D (either 4.8 or 6.0 mg/kg).

Efficacy Data. In the completed phase 1 dose escalation study, A166 demonstrated promising anti-tumor activity across dose levels from 0.1 to 6 mg/kg with five patients achieving PR and a DCR of 45.5% in the 25 patients who underwent at least one efficacy assessment.

In the ongoing phase 1 dose expansion study, as of the data cut-off date (July 13, 2022), 58 patients enrolled in the 4.8 and 6.0 mg/kg A166 cohorts were evaluable for response assessment, all of whom had prior HER2-targeted therapy with a median four lines of prior treatments, including 100% (58/58) received trastuzumab, 94.8% (55/58) received anti-HER2 TKIs, 32.8% (19/58) received pertuzumab, and 20.7% (12/58) received anti-HER2 ADCs in which eight received T-DM1, three received ARX-788 (HER2 ADC) and one received TAA-013 (HER2 ADC).

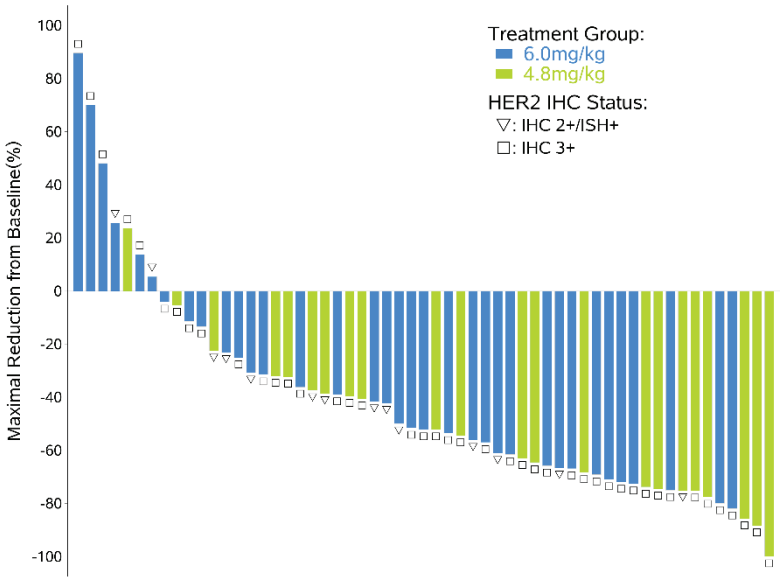
As illustrated in the table below, A166 achieved an overall ORR of 70.7% (41/58), with an ORR of 73.9% (17/23) in the 4.8 mg/kg cohort and 68.6% (24/35) in the 6.0 mg/kg cohort. The median PFS was 12.3 months in the 4.8 mg/kg cohort and 9.4 months in the 6.0 mg/kg cohort. The median DOR was 11.0 months in the 4.8 mg/kg cohort and 8.3 months in the 6.0 mg/kg cohort.

Best Responses for HER2+ BC Patients in 4.8 and 6.0 mg/kg Cohorts

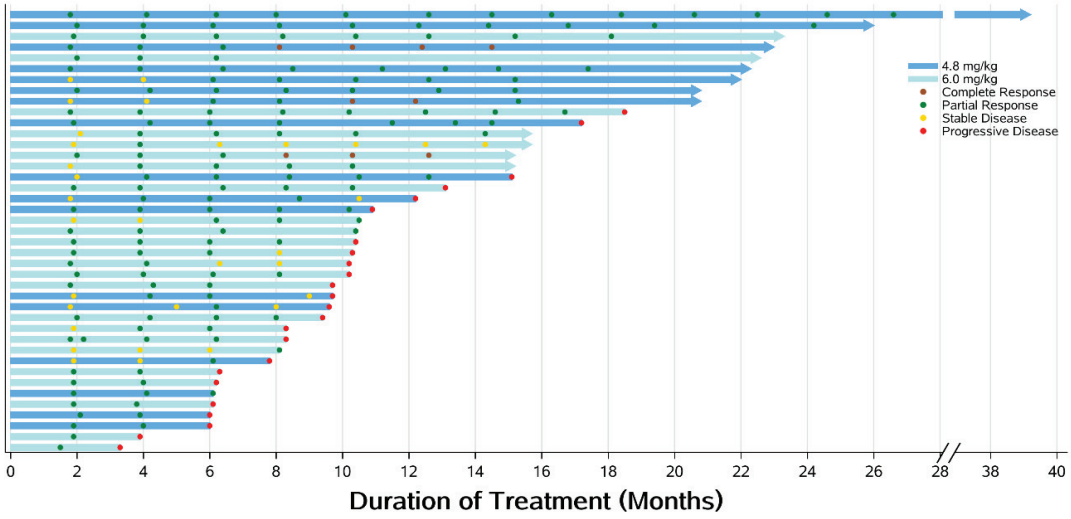
	4.8 mg/kg (N=23)	**6.0 mg/kg (N=35)**	**Total (N=58)**
ORR	73.9%	68.6%	70.7%
DCR	82.6%	80.0%	81.0%
mPFS (months)	12.3	9.4	10.2
mDOR (months)	11.0	8.3	8.5

Abbreviations: CR, complete response; PR, partial response; ORR, objective response rate (CR + PR); DCR, disease control rate (CR + PR + SD); mPFS: median PFS; mDOR: median duration of response

The below waterfall plot shows the best percent change from baseline in target lesions for each evaluable patient who had PR or CR.



The swimmer plot below shows the durable objective responses and disease stabilization of the patients who achieved PR or CR. Overall, these results demonstrated the encouraging anti-tumor activity of A166 in heavily pretreated HER2+ BC patients, highlighted by an ORR of 73.9% at RP2D (4.8 mg/kg) and median PFS of more than 12 months.



Safety Data. In the completed dose escalation study, A166 was generally safe and well-tolerated with no incidence of dose-limiting toxicities observed in all dose cohorts. In the dose expansion study, as of the data cut-off date (February 28, 2022), 77 patients were evaluable for safety assessment. TRAEs were primarily ocular and peripheral nerve-related and reversible. Grade 3 or above TRAEs were reported in 61.0% (47/77) of patients. The following table illustrates the TRAEs that occurred in 10% or more patients.

Most common TRAEs (any grade and grade ≥ 3)

TRAEs	4.8 mg/kg (N=29)		6.0 mg/kg (N=48)		Total (N=77)	
No. of Patients (%)	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Overall	29 (100)	16 (55.2)	48 (100)	31 (64.6)	77 (100)	47 (61.0)
Corneal epitheliopathy	28 (96.6)	11 (37.9)	45 (93.8)	17 (35.4)	73 (94.8)	28 (36.4)
Blurred vision	24 (82.8)	7 (24.1)	42 (87.5)	12 (25.0)	66 (85.7)	19 (24.7)
Peripheral neuropathy	17 (58.6)	1 (3.4)	25 (52.1)	4 (8.3)	42 (54.5)	5 (6.5)
Dry eyes	10 (34.5)	3 (10.3)	21 (43.8)	9 (18.8)	31 (40.3)	12 (15.6)
Muscular weakness	11 (37.9)	1 (3.4)	11 (22.9)	2 (4.2)	22 (28.6)	3 (3.9)
Alopecia	3 (10.3)	0	16 (33.3)	0	19 (24.7)	0
Anemia	4 (13.8)	0	14 (29.2)	3 (6.3)	18 (23.4)	3 (3.9)
Creatine phosphokinase increased	8 (27.6)	0	10 (20.8)	0	18 (23.4)	0
Myoglobin blood increased	6 (20.7)	0	9 (18.8)	0	15 (19.5)	0
ALT increased	6 (20.7)	0	8 (16.7)	0	14 (18.2)	0
AST increased	6 (20.7)	0	8 (16.7)	0	14 (18.2)	0
Hypomagnesemia	8 (27.6)	0	5 (10.4)	0	13 (16.9)	0
Leukopenia	1 (3.4)	0	10 (20.8)	2 (4.2)	11 (14.3)	2 (2.6)
Hyponatremia	4 (13.8)	0	5 (10.4)	1 (2.1)	9 (11.7)	1 (1.3)
Proteinuria	3 (10.3)	0	6 (12.5)	0	9 (11.7)	0
Blood bilirubin increased	4 (13.8)	0	4 (8.3)	0	8 (10.4)	0

Note:

(1) Most common TRAEs include TRAEs of any grade with an incidence ≥ 10% and all grade 3 or above TRAEs.

All ocular-related AEs were reversible and occurred approximately after two cycles of A166 treatment, and the majority were grade 1 or grade 2, which were easy to diagnose clinically and assess severity through protocol-assigned eye examinations. Throughout the trial, we followed an optimized eye care management protocol. Patients prophylactically received artificial tears, ocular lubricants and eyedrops, according to ophthalmologist's discretion, depending on the occurrence or grading of epitheliopathy. Treatment delay and dose reduction were used for grade 3 or 4 ocular-related AEs. In addition, unplanned visits were encouraged in the protocol in case ocular symptoms appeared or deteriorated. Using this strategy, A166-related corneal epitheliopathy was generally manageable and reversible in our patients.

PK Data. A166 demonstrated high stability in blood circulation with the exposure and maximum plasma concentration of the serum free payload duostatin-5 amounting to only 0.1% and 0.2%, respectively, as that of the total A166 ADC in the first week of administration.

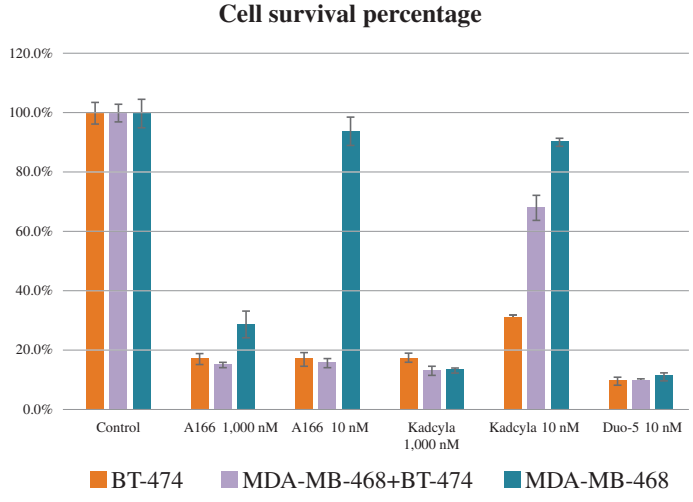
Conclusion. A166 demonstrated promising anti-tumor efficacy in previously treated advanced HER2+ solid tumors, highlighted by its rapid and durable anti-tumor activity in heavily pre-treated advanced HER2+ BC patients. It also exhibited a differentiated safety profile with high stability in blood circulation.

Summary of Preclinical Data

We performed a series of *in vitro* and *in vivo* preclinical studies to characterize the potency, toxicology, and pharmacological properties of A166.

In non-head-to-head comparison with DM-1, i.e., payload of Kadcyla, duostatin-5 demonstrated a higher *in vitro* cytotoxicity, indicated by its lower half maximal inhibitory concentration (IC_{50}) value (3.4 nM for duostatin-5 vs 14.94 nM for DM-1).

In a head-to-head cell viability and proliferation study, A166 demonstrated a stronger HER2-directed anti-tumor effect compared with Kadcyla. As shown in the diagram below, treatment with A166 (10 nM) led to an over 80% reduction in the viability of BT-474, a HER2+ BC cell line, which was near two-fold greater than that achieved by Kadcyla. Notably, A166 (10 nM) treatment also resulted in a similarly significant viability reduction in HER2– BC cell line MDA-MB-468 cocultured with BT-474, whereas Kadcyla (10 nM) treatment only led to a modest viability reduction in the cocultured cells. This suggested that A166 may have a greater bystander killing capability than Kadcyla. Importantly, A166 did not affect the viability of MDA-MB-468 when cultured alone, suggesting that the bystander killing of A166 is only effective in HER2– cells that neighbor HER2+ cells, indicating low potential for systemic toxicity.



Furthermore, *in vivo* PK-PD analysis demonstrated high stability of A166 in systemic circulation with free payload detected only in the target tissue but not in the systemic circulation in a dose-dependent manner. This result potentially contributed to the favorable toxicology profiles of A166 in rat and cynomolgus monkey studies, in which A166's toxicities were observed in fewer organs (eyeball, lung, spleen, thymus gland and bone marrow) in non-head-to-head comparison with those of Kadcyla (liver, spleen, thymus gland, skin, tongue, sciatic nerve, spinal cord, lung and kidney) and Enhertu (intestine, lung, skin, testicle, bone marrow and kidney).

Material Communications and Next Steps

We received IND approval from the NMPA in April 2018 for initiating A166's phase 1 clinical trial for advanced HER2+ solid tumors in China. We completed the phase 1a dose escalation part of the phase 1 clinical trial in April 2020. Taking into the industry practice as advised by Frost & Sullivan and as advised by PRC Legal Advisers with respect to PRC laws and regulations, the phase 1a dose escalation study was a completed clinical trial with its main purpose aligning with the overall purpose of a conventional phase 1 trial, and therefore the completion of the phase 1a dose escalation study is equivalent to the completion of a conventional phase 1 trial. We consulted with the CDE in March 2021 and received their approval in June 2021 for commencing the pivotal phase 2 trial for advanced HER2+ BC in China. We initiated pre-NDA consultation with the NMPA in December 2022 regarding the NDA submission of A166 as a 3L+ treatment for patients with advanced HER2+ BC and received feedback from the CDE's clinical division in February 2023 agreeing for us to submit an NDA under priority review, based on results from the primary analysis of the ongoing pivotal phase 2 trial which showed that A166 has met the primary endpoints. We submitted an NDA to the NMPA in May 2023. Pending consultation with the CDE, we plan to commence a confirmatory phase 3 clinical trial to explore A166 as a 2L+ treatment for advanced HER2+ BC in the second half of 2023.

The table below sets forth the timeline of preclinical studies and clinical trials for A166.

Milestone/Stage	Timeline	Hospital sites	Principal investigator(s)
Preclinical development (PCC to IND-enabling stage)	July 2015 – August 2017	N/A	N/A
IND approval	China: April 2018	N/A	N/A
Phase 1 trial for advanced HER2+ solid tumors (including BC, NSCLC, GC, CRC and others): dose escalation study	August 2018 – April 2020	3	Hu Xichun, MD
Phase 1 trial for advanced HER2+ solid tumors: dose expansion study	May 2020 – ongoing	3	Hu Xichun, MD
Pivotal phase 2 trial for advanced HER2+ BC	August 2021 – ongoing	39	Hu Xichun, MD
Confirmatory phase 3 trial for advanced HER2+ BC	Expected to be commenced in the second half of 2023	N/A	N/A
Phase 1b trial for advanced HER2+ GC	December 2021 – ongoing	20	Liu Tianshu, MD
Phase 1b trial for advanced HER2+ CRC	December 2021 – ongoing	21	Xu Ruihua, MD

As of the Latest Practicable Date, we had received no major concerns or objections from the NMPA to our clinical development plans for A166.

A166 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

SKB315 – A CLDN18.2 ADC

Overview

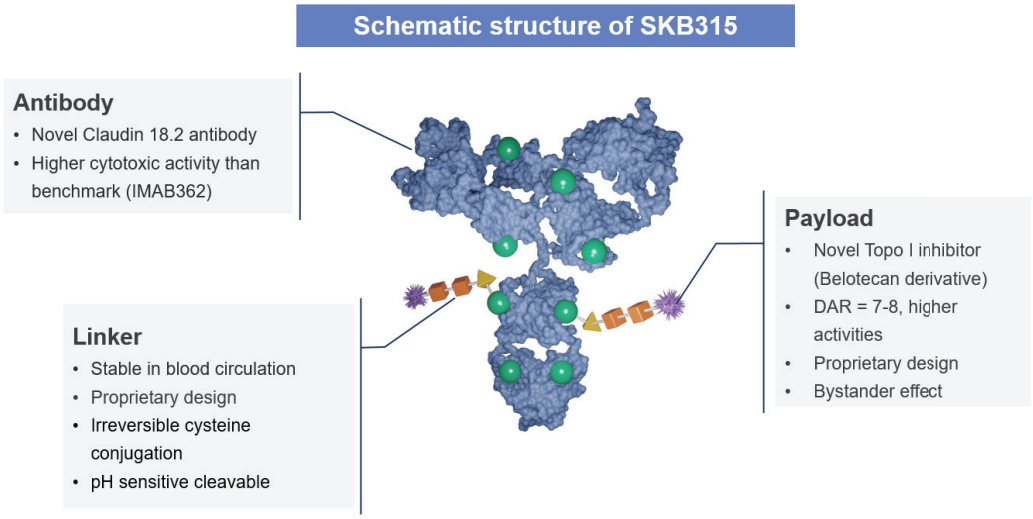
SKB315 is a novel CLDN18.2 ADC designed for treating advanced solid tumors. CLDN18.2 is highly expressed in prevalent and lethal cancers with limited effective treatments such as GC and PC, while its normal expression is restricted to gastric mucosa. This selective expression makes CLDN18.2 a promising drug target, highlighted recently by the positive clinical results of zolbetuximab, a CLDN18.2 mAb in phase 3 stage as of the Latest Practicable Date. Compared with mAbs, targeting CLDN18.2 via ADC is potentially a more efficacious therapeutic strategy as ADCs exert anti-tumor effects primarily via cytotoxic payloads and bystander effect, which may overcome low or heterogeneous CLDN18.2 expression in tumors that traditionally limits the efficacy of mAbs. With a differentiated payload-linker design and an in-house developed humanized CLDN18.2 antibody, SKB315 demonstrated encouraging efficacy and safety across various preclinical *in vivo* tumor models with heterogeneous CLDN18.2 expression, indicating its promising therapeutic potential.

In June 2022, we entered into a license and collaboration agreement with MSD, under which we granted MSD exclusive global development and commercialization rights for SKB315. Pursuant to this agreement, we are carrying out certain activities in support of SKB315's clinical development, including an ongoing phase 1a clinical trial of SKB315 in patients with advanced solid tumors in China, which we initiated in February 2022 and expect to complete in the second half of 2024. See "– Our License and Collaboration Arrangements – License and Collaboration Agreement with MSD for SKB315" for details.

Drug Design and Mechanism of Action

CLDN18.2 belongs to a family of proteins that maintain cell junctions controlling the interchange of molecules between cells. In normal tissues, CLDN18.2 is selectively expressed in the gastric mucosa, i.e., the innermost layer of the stomach wall, making it largely inaccessible to targeting antibodies. However, the disrupted cell junctions during cancer development expose CLDN18.2 on the tumor cell surface, allowing it to be targeted by antibodies. This tumor specificity makes CLDN18.2 an attractive anti-tumor target in various cancers, such as GC and PC, where CLDN18.2 is highly expressed.

SKB315 is a novel CLDN18.2 ADC that aims to deliver cytotoxic drugs selectively to CLDN18.2-expressing tumor cells, with an optimized design to maximize efficacy and safety. The core components and innovative features of SKB315 are illustrated below.



SKB315 is configured with a proprietary, in-house developed humanized CLDN18.2 mAb and a differentiated payload-linker design. Mechanistically, SKB315 is guided by the CLDN18.2 mAb to the CLDN18.2-expressing tumor cells, where it exerts targeted cell killing, bystander killing and immune-mediated killing via mechanisms.

Market Opportunity and Competition

CLDN18.2 overexpression has been identified in various cancers, such as GC and PC, indicating the potential of CLDN18.2 ADCs for treating a wide range of cancers. For more details regarding the addressable market size of CLDN18.2 ADCs, see "Industry Overview – Global CLDN18.2 ADC Market – Addressable Market Size of CLDN18.2 ADCs."

Competitive Advantages

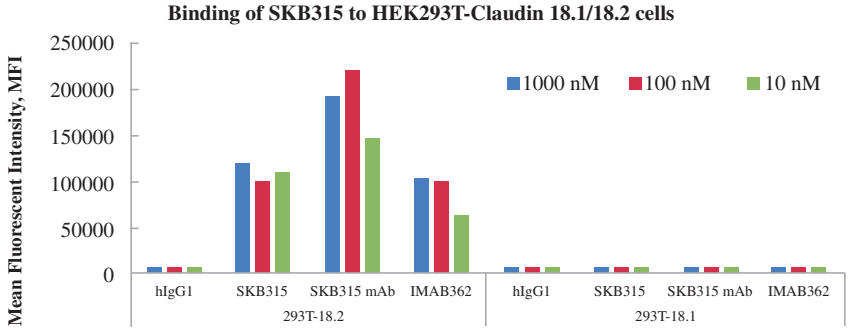
Differentiated Payload-linker Design. SKB315 is configured with a differentiated payload-linker design in which a novel, moderately cytotoxic topoisomerase I (TOPO1) inhibitor is conjugated at a high DAR to the targeting antibody. Our differentiated payload-linker design is potentially less harmful to gastric tissues where CLDN18.2 is expressed. SKB315 exhibited a good safety profile in mouse and cynomolgus monkey models where it showed a broad therapeutic window with limited and reversible organ toxicities, indicating a potentially promising safety profile in humans.

Therapeutic Potential against Tumors with High to Low CLDN18.2 Expression. Equipped with a differentiated payload-linker design and an in-house developed CLDN18.2 antibody, SKB315 demonstrated comparable CLDN18.2 specificity, comparable or greater CLDN18.2 affinity and greater proliferation inhibitory effect across multiple cancer cell lines compared with zolbetuximab in head-to-head *in vitro* studies. These features potentially contributed to SKB315's strong anti-tumor activities in various preclinical *in vivo* tumor models with high to low CLDN18.2 expression, indicating the therapeutic potential of SKB315 for treating tumors across a wide range of CLDN18.2 expression.

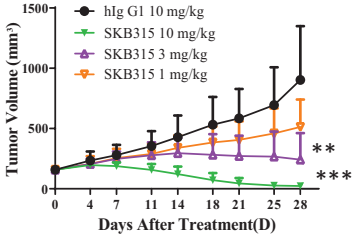
Summary of Preclinical Data

We have evaluated SKB315 in a series of preclinical studies, including (i) mechanism of action studies, (ii) PD studies *in vitro* and *in vivo* for anti-tumor activity evaluation, (iii) *in vitro* and *in vivo* PK studies of SKB315, its payload and antibody to elucidate their patterns of absorption, distribution, metabolism and excretion, and (iv) *in vitro* and *in vivo* studies to evaluate the safety of SKB315 and its payload molecule, including single-dose toxicity, repeated-dose toxicity and other toxicological assays. Notably, in a series of head-to-head preclinical studies compared with zolbetuximab (under the drug code of IMAB362) as shown in the diagrams below, SKB315 demonstrated comparable CLDN18.2 binding specificity and comparable or greater CLDN18.2 binding affinity.

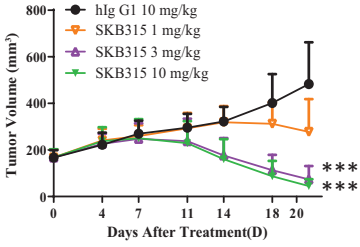
Binding Affinity and Specificity of SKB315 for Injection to Human Claudin 18.1/18.2 at the Cellular Level



SKB315 has demonstrated promising in vivo efficacy, highlighted by its anti-tumor activities in CLDN18.2+ GC PDX model and CLDN18.2-low GC PDX model, as shown in the diagrams below.



Gastric Cancer
PDX-GA0006
CLDN18.2 +++
***i.v.*, BIW*4**



Gastric cancer
PDX-GA6844
CLDN18.2+
***i.v.*, BIW×3**

Moreover, in a cynomolgus monkey model, which is a non-human primate model that closely resembles human, treatment with SKB315 at the highest non-severely toxic dose, which refers to the highest dose level that does not result in lethal, life-threatening or irreversible toxicities, did not result in GI or haematological toxicities, with reversible thymic lymphocyte reduction being the only detectable toxicity.

SKB315 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

Preclinical ADC Assets

Building on our sophisticated ADC platform and accumulated expertise from the development of clinical-stage ADCs, we are advancing over ten preclinical ADC assets that are well positioned to deliver enhanced anti-tumor efficacy and superior safety results. Furthermore, they strategically cover high potential targets with a demonstrated role in cancer pathogenesis, with a focus on cancers with significant patient populations and for which there are limited or no effective treatments.

A410 is one of our preclinical-stage ADC candidates. As of the Latest Practicable Date, there were no ADCs approved by the NMPA targeting the same tumor associated antigen (TAA) as A410. Utilizing a differentiated payload-linker strategy, A410 is equipped with a moderately toxic payload that potentially reduces toxicities, with improved therapeutic window and safety profile demonstrated in preclinical studies compared to the latest non-head-to-head data publicly available for an FDA-approved ADC targeting the same TAA. We received IND approval from the NMPA for A410 in February 2023.

In December 2022, we entered into an exclusive license and collaboration agreement with MSD to develop up to seven preclinical ADC assets. Under this agreement, we granted MSD exclusive global licenses to research, develop, manufacture and commercialize multiple ADC assets and exclusive options to obtain additional exclusive licenses to certain other ADC assets. We retain the right to research, develop, manufacture and commercialize certain licensed and option ADCs for China, Hong Kong and Macau. For details, see "– Our License and Collaboration Arrangements – License and Collaboration Agreement with MSD for Up to Seven Preclinical ADC Assets."

OUR PRECLINICAL ADC ASSETS MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies)

A167 – A PD-L1 mAb

Overview

A167 is a humanized mAb that targets PD-L1, an important immune checkpoint protein. Targeting PD-L1 and its receptor PD-1 has become the cornerstone of cancer immunotherapy, with PD-(L)1 mAbs now widely recognised as a front-line cancer immunotherapy agent. To further elicit the anti-tumor activity of PD-(L)1 mAbs, the market has witnessed encouraging clinical development advancement of PD-(L)1 mAbs-based combination strategies in recent years, with an aim to achieve synergistic efficacies, boost response rates, overcome heterogeneity across patients, and relieve treatment resistance.

Against this backdrop, we have developed A167 as the backbone of our immunotherapy franchise, not only as a monotherapy but, more importantly, to be used in combination with our ADCs and other oncology assets. Building on its robust efficacy and safety results in multiple monotherapy trials for advanced solid tumors such as RM-NPC, A167 in combination with SKB264 demonstrated encouraging preliminary efficacy in an ongoing phase 2 trial conducted in China, highlighted by an ORR of 85.7% in first-line advanced TNBC patients. A167's promising clinical results underscore its therapeutic potential as monotherapy and combination therapies.

We filed an NDA with the NMPA in November 2021 and expect to receive conditional approval in the second half of 2023 or the first half of 2024 to market A167 as a 3L+ treatment for RM-NPC. This approval, if granted, will be conditional partly upon our commitment to complete a phase 3 trial of A167 in combination with chemotherapy as a first-line treatment for RM-NPC, for which we had completed patient enrollment as of the Latest Practicable Date. Moreover, we are actively exploring A167's potential as an early-line treatment in combination with our ADC assets to maximize the clinical value of our oncology franchise, beginning with two ongoing phase 2 trials – a phase 2 trial of SKB264 in combination with A167 with or without chemotherapy, as an early-line treatment for advanced EGFR-wild type and EGFR-mutant NSCLC and a phase 2 trial of SKB264 with or without A167 as a first-line treatment for advanced TNBC.

In August 2018, we granted to Harbour BioMed an exclusive, royalty-bearing, sublicensable license to develop, manufacture and commercialize A167 outside Greater China. For details, see "License and Collaboration Arrangements – Collaboration and Licensing Agreement with Harbour Biomed for A167." See also "Connected Transactions – Non-exempt Continuing Connected Transaction – Licensing Agreement" for details on our patent and technology in-license agreement with Kelun Research Institute, a wholly-owned subsidiary of Kelun Pharmaceutical, in relation to A167.

Mechanism of Action

Programmed cell death ligand-1 (PD-L1) is a transmembrane protein that functions as a brake of T-cell activation via its binding to two proteins, i.e., programmed cell death-1 (PD-1) expressed mainly on activated T cells and the cluster of differentiation 80 (B7-1) protein expressed on antigen-presenting cells. The interaction of PD-L1 with PD-1 or B7-1 produces an inhibitory signal that suppresses T cell proliferation and function, which is a major immune checkpoint that helps keep immune responses in check. However, this checkpoint is often exploited by tumor cells to evade immune detection and elimination. In particular, PD-L1 is overexpressed by various cancers and certain immune cells in the tumor microenvironment (TME), contributing to an immunosuppressive TME that is favorable for tumor growth.

By modulating the interaction between immune cells and tumor cells, immune checkpoint inhibitors, such as PD-(L)1 mAbs, have become an important class of anti-cancer treatment. As a PD-L1 mAb, A167 selectively binds to PD-L1 and inhibits the association of PD-L1 with PD-1 and B7-1, thereby reawakening the suppressed anti-tumor immune response. A167 is a human IgG1 mAb with a silenced constant fragment (Fc) region to deliberately remove ADCC and complement-dependent cytotoxicity (CDC), i.e., two immune-mediated cell killing functions, to minimize toxicity towards healthy tissues.

Market Opportunity and Competition

RM-NPC. NPC is a type of head and neck cancer that starts in the nasopharynx, i.e., the upper part of the throat behind the nose and near the base of the skull. According to Frost & Sullivan, the incidence of NPC in China increased from 59.5 thousand in 2017 to 64.0 thousand in 2022 and is expected to reach 69.1 thousand in 2030. Patients with RM-NPC account for approximately 35% of total NPC cases.

In China, the early-line treatments for RM-NPC primarily involve repeat radiotherapy (for recurrent NPC), chemotherapy and PD-1 inhibitors. The current standard of care only offers modest therapeutic benefits, with the effective rates of PD-1 mAb monotherapy ranging from approximately 20% to 30%. Given that PD-L1 is expressed in about 89% to 95% of NPC tumors, PD-L1 blockade by PD-L1 mAb is a promising therapeutic strategy to expand the currently limited treatment options for RM-NPC. As of the Latest Practicable Date, there were no PD-L1 mAbs approved by the NMPA for treating RM-NPC in China. Our NDA-filed A167 was the only PD-L1 mAb in phase 1 or beyond for treating RM-NPC in China as of the same date. For details regarding the competitive landscape of PD-(L)1 mAbs for RM-NPC in China, see "Industry Overview – China's PD-(L)1 mAb Market – China's PD-(L)1 MAb Market – Competitive Landscape of PD-(L)1 MAbs for RM-NPC."

Competitive Advantages

Significant early-line Potential in Combination Strategies. Combination strategies of PD-(L)1 mAbs with other cancer therapies have potential to improve clinical outcome compared with their monotherapy counterparts. As the backbone of our immunotherapy franchise, A167 enables us to formulate combination strategies with our other oncology assets such as SKB264. The targeted tumor killing by ADCs and antibodies, in particular, is expected to generate a stimulatory signal that draws T cells towards the tumor site, thus facilitating A167 to inhibit the PD-(L)1 checkpoint and expose tumor cells to immune attacks. Our combination strategies for SKB264 and A167 allow us to explore patients in earlier treatment lines with potentially greater efficacy, beginning with TNBC and NSCLC. Based on preliminary results from a phase 2 trial conducted in China, A167 in combination with SKB264 demonstrated a promising ORR of 85.7% as a first-line therapy in advanced TNBC patients, indicating the therapeutic potential of A167 as the backbone of our combination strategies. For more details of A167's combination strategies, see "– Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A167 – Next Steps."

Promising Anti-tumor Efficacy and Safety Profile. A167 demonstrated a promising clinical efficacy and safety profile in advanced solid tumors, highlighted by an ORR of 26.5% in its pivotal phase 2 trial in RM-NPC patients, which was comparable to approved PD-1 inhibitors AiRuiKa (camrelizumab) (28.3%) and Tuoyi (toripalimab) (23.9%), the only two domestically developed PD-1 inhibitors approved for 3L+ RM-NPC in China, as demonstrated in the diagram below.

Moreover, A167 demonstrated a good safety profile in all completed clinical trials, with the types and occurrences of AEs comparable to those of approved PD-(L)1 mAbs. Notably, based on the latest non-head-to-head data publicly available, the incidence of immune-related adverse events (irAEs) to A167 was comparable or lower compared to those of AiRuiKa and Tuoyi, as shown in the table below. These clinical trial results underscore A167's therapeutic potential as the backbone of our immunotherapy franchise and support A167's position as the first PD-L1 mAb expected to be approved for treating RM-NPC in China.

	A167 (N = 398)	**AiRuiKa (N = 1,520)**	**Tuoyi (N = 943)**
	irAE incidence (%)		
Pneumonia	1.0	4.5	2.5
Hepatitis	1.0	10.5	3.8
Diarrhea or Colitis	0.3	1.3	0.3
Nephritis	0	2.3	0.4
Myocarditis	0.5	0.2	0.3
Myositis	0	0.06	0.2
Pancreatitis	0	1.1	0.5
Skin adverse reactions	4.5	8.8	3.9
Thrombocytopenia	0.8	1.1	1.3
Endocrine abnormalities			
Hypothyroidism	13.6	25.4	14.5
Hyperthyroidism	5.8	7.8	6.4
Thyroiditis	0.3	0.3	0.5
Hypophysitis	0	0.2	N/A
Adrenal insufficiency	0	0.6	0.5
Pituitary insufficiency	0	N/A	0.3
Hyperglycemia and diabetes	0.8	1.9, 0.6[(1)]	2.2

Notes:

(1) AiRuiKa's incidence of hyperglycemia is 1.9% and that of diabetes is 0.6%.

Sources: AiRuiKa: AiRuiKa's drug label; Tuoyi: Tuoyi's drug label

Clinical Development Plan

We are advancing the clinical development of A167 as the backbone of our immunotherapy franchise, both as a monotherapy and combination therapy with our ADCs and other oncology assets. We initiated a phase 1a clinical trial for advanced solid tumors and a pivotal phase 2 trial for RM-NPC in China in December 2017 and January 2019, respectively, and completed these two trials in April 2022 and January 2022, respectively. We are conducting a phase 3 trial of A167 in combination with chemotherapy as a first-line treatment for RM-NPC, as well as two phase 2 trials of A167 in combination with SKB264 for advanced NSCLC (with or without chemotherapy) and advanced TNBC, respectively. The table below sets forth our clinical development plan for A167:

Indication	Mono-/Combo-therapy	Location	Trial phase/ designation	Trial status	(Expected) Trial start date	Expected trial end date
RM-NPC	Combo with chemo (cisplatin and gemcitabine)	China	Phase 3	Ongoing	March 2022	2H 2025
Advanced NSCLC	Combo with SKB264 ± platinum-based chemo	China	Phase 2	Ongoing	May 2022	2H 2024
Advanced TNBC	Combo with SKB264	China	Phase 2	Ongoing	July 2022	1H 2025

Summary of Clinical Trial Data

After receiving IND approval in September 2017, we have completed several clinical trials of A167 in China, covering multiple indications including advanced solid tumors and RM-NPC. Set forth below is a summary of the key data from A167's completed and ongoing clinical trials.

Phase 3 Clinical Trial for RM-NPC

This is a multi-center, double-blind, randomized, placebo-controlled trial to evaluate the safety and efficacy of A167 in combination with cisplatin and gemcitabine as a potential first-line treatment for patients with RM-NPC. This trial plans to enroll 291 patients across 39 clinical research centers in China.

Trial Objectives. The primary endpoint is the IRC-assessed PFS based on RECIST 1.1. The secondary endpoints include the PFS assessed by Investigator Assessment according to RECIST 1.1, the ORR, DCR, DOR and TTR assessed by the IRC and trial investigators based on RECIST 1.1, OS (1-year and 2-year), the levels of ADA before and after drug administration, and the safety and PK of A167.

Trial Progress. Patient enrollment of this trial had been completed as of the Latest Practicable Date.

Trial Design. Subjects are randomized 2:1 to receive either combinations of 1200 mg of A167, 80 mg/m^2 of cisplatin and 1000 mg/m^2 of gemcitabine, or placebo, administered intravenously once every three weeks until there is confirmed disease progression, intolerable toxicity, or withdrawal of informed consent.

Pivotal Phase 2 Clinical Trial for RM-NPC

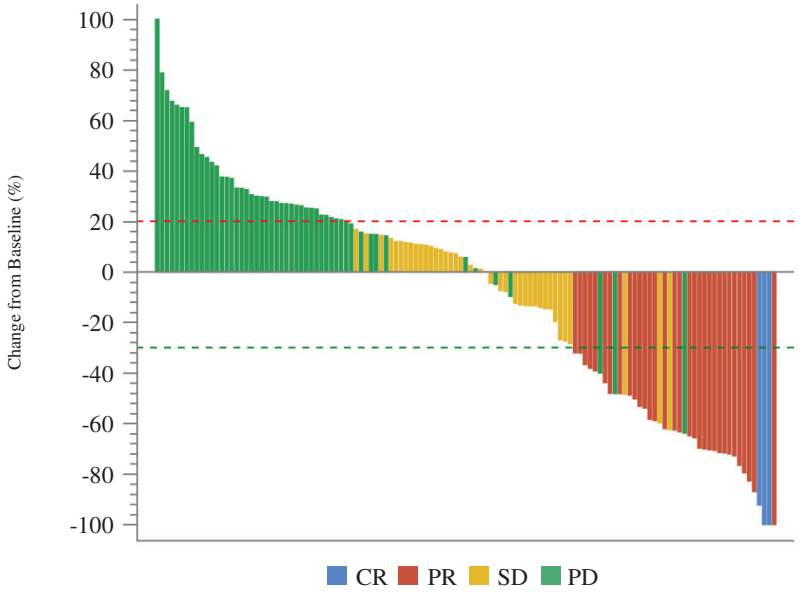
This was an open-label, multi-center, single-arm trial to evaluate the safety and efficacy of A167 in patients with RM-NPC. This trial was conducted in 153 patients across 44 clinical research centers in China.

Trial Objectives. The primary endpoint was the IRC-assessed ORR based on RECIST 1.1. The secondary endpoints were the ORR by Investigator Assessment according to RECIST 1.1 and immune-related response evaluation criteria in solid tumors, PFS, OS, DCR, DOR, TTR, and the PK, immunogenicity, safety of A167.

Trial Progress. This trial was completed in January 2022.

Trial Design. Subjects received 900 mg of A167, administered intravenously once every two weeks until there was confirmed disease progression, intolerable toxicity, or withdrawal of informed consent.

Efficacy Data. A167 elicited an ORR of 26.5% in the 132 patients who had at least one efficacy assessment, among whom three patients had CR, 32 had PR, 40 had SD and 51 had PD, as illustrated in the waterfall plot below. The median PFS, DOR, and OS were 2.8 months, 12.6 months, and 15.3 months, respectively. The below waterfall plot shows the best percentage change from baseline in target lesions for each evaluable patient.



Safety Data. 115 (75.2%) patients experienced at least one TRAE. The most common (≥10%) TRAEs included hypothyroidism (24.8%), anemia (13.1%) and leukopenia (10.5%). Grade 3 or above TRAEs occurred in 24 (15.7%) patients, among which 8 (5.2%) patients experienced treatment-related SAEs. Seventeen (11.1%) patients died due to AEs, which were considered by the trial investigator to be unrelated to the study drug. Four (2.6%) patients experienced study drug-related AEs leading to permanent discontinuation. 32 (20.9%) patients experienced irAEs, of which six (3.9%) patients had grade 3 or higher irAEs.

Conclusion. A167 demonstrated encouraging anti-tumor efficacy in RM-NPC patients with a manageable safety profile.

Phase 1a Clinical Trial for Advanced Solid Tumors

This was an open-label, multi-center, single-arm trial to evaluate the safety and tolerability of A167 in patients with locally advanced or metastatic solid tumors and to determine the RP2D of A167. This trial was conducted in 102 patients across eight clinical research centers across China.

Trial Objectives. The primary endpoints were the safety and tolerability of A167. The secondary endpoints were A167's PK, receptor occupancy (i.e., the degree of occupancy of A167 on cell-surface PD-L1), immunogenicity, preliminary efficacy, and biomarkers.

Trial Progress. This trial was completed in April 2022.

Trial Design. Subjects received 600, 900, 1,200, 1,500, or 1,800 mg of A167 once every 14 days or once every 21 days until there was confirmed disease progression, intolerable toxicity, or withdrawal of informed consent.

Efficacy Data. A167 demonstrated an ORR of 15.69% and DCR of 60.78% in 102 patients with locally advanced or metastatic solid tumors. The results of the subgroup analyses are shown in the table below:

Subgroup	**ORR**	**DCR**
NPC	28.57% (2/7)	71.43% (5/7)
HNSCC	27.27% (3/11)	54.55% (6/11)
CC	25.00% (4/16)	62.50% (10/16)
Liver cancer	13.64% (3/22)	72.73% (16/22)
LC	7.89% (3/38)	55.26% (21/38)

Safety Data. A167 exhibited manageable safety in patients with advanced solid tumors who received an escalating dose of A167 injection up to 1800 mg once every 21 days. 87 (85.3%) patients had at least one TRAE. The most common (≥20% incidence rate) TRAEs were increased blood thyroid stimulating hormone (TSH) (23.5%), increased aspartate aminotransferase (21.6%) and increased alanine aminotransferase (21.6%). Grade 3 or above TRAEs occurred in 17 (16.7%) patients, among which seven patients had treatment-related SAEs. AEs led to death in 11 (10.8%) patients, among which ten patients died due to AEs that were considered by the trial investigator to be unrelated or possibly unrelated to the study drug, while one patient died due to pulmonary inflammation that was considered by the trial investigator to be probably related to the study drug.

Conclusion. A167 demonstrated encouraging anti-tumor efficacy in a range of advanced solid tumors with a manageable safety profile.

Next Steps

We submitted an NDA to the NMPA for A167 as a 3L+ treatment for RM-NPC in November 2021 based on our pivotal phase 2 trial results, which met the primary endpoint pre-specified by the NMPA, and expect to receive conditional approval in the second half of 2023 or the first half of 2024.

In parallel, we have positioned A167 as the cornerstone for combination therapies with other assets in our pipeline to exploit the potential synergy between immune-oncology and ADC/targeted therapy. We are conducting two phase 2 trials in China to evaluate the combination potential of A167 and SKB264 as a 1L treatment for advanced NSCLC (with or without chemotherapy) and advanced TNBC.

A167 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

A140 – An EGFR mAb

Overview

We are developing A140, an EGFR mAb, as a cetuximab biosimilar. Cetuximab, in combination with chemotherapy, is approved by the NMPA for treating mCRC with wild-type RAS, an oncogene, and RM-HNSCC in China. In combination with radiotherapy, cetuximab is also approved in China for treating LA-HNSCC. In 2018, cetuximab was included in the NRDL through price negotiation. Driven by its high demand in China and NRDL inclusion, cetuximab posted annual sales of approximately €441 million in the Asia-Pacific region in 2022. The patent protection for cetuximab in China expired in 2017. While a number of biotech companies in China are developing cetuximab biosimilars, none had been approved as of the Latest Practicable Date.

A140 has the potential to be the first cetuximab biosimilar approved in China, providing increasing accessibility and affordability to an underserved patient population. It demonstrated PK bioequivalence to cetuximab in a phase 1 clinical trial, with a pivotal phase 3 clinical equivalence trial for RAS wild-type mCRC underway. Notably, according to Frost & Sullivan, A140 is the first cetuximab biosimilar candidate in China to adopt a phase 3 head-to-head trial design that strictly follows the CDE's Guidelines for Design of Clinical Trials of Injectable Cetuximab Biosimilar (for Trial Implementation) ("Cetuximab Biosimilar Guidelines"), which potentially translates into an accelerated review process.

We plan to file an NDA with the NMPA in the second half of 2023 for RAS wild-type mCRC. With cetuximab in the NRDL, A140, upon its anticipated NMPA approval, is expected to be automatically admitted into the NRDL, potentially facilitating A140's market penetration as a potential first cetuximab biosimilar. Further, we will follow the CDE's "Technical Guidelines for Similarity Evaluation and Indication Extrapolation of Biosimilars" (《生物類似藥相似性評價和適應症外推技術指導原則》) to explore the opportunities of A140 for treating other indications for which cetuximab has been already approved, including RM-HNSCC and LA-HNSCC, as well as indications for which cetuximab is currently under clinical development in China, such as NSCLC.

Background of Reference Drug

Cetuximab was developed by the Weizmann Institute of Science, one of the world's top-ranking multidisciplinary research institutions. Since its first FDA approval under the brand name Erbitux in 2004, cetuximab in combination with chemotherapy has been approved as an early-line treatment for RAS wild-type, EGFR-expressing mCRC, BRAF V600E-mutated mCRC and RM-HNSCC and in combination with radiotherapy for LA-HNSCC in various countries, including the U.S., EU, and China. Cetuximab is also under clinical trials for other indications across the world, such as NPC, NSCLC and cutaneous squamous cell carcinoma (cSCC). In China, cetuximab was first approved by the NMPA as a 2L treatment for mCRC in 2005. It was then approved as a first-line treatment in combination with chemotherapies for RAS wild-type mCRC in 2019, and in combination with chemotherapies as a first-line treatment for RM-HNSCC in 2020. In 2022, cetuximab, in combination with radiotherapy, was approved by the NMPA as a first-line treatment for LA-HNSCC. According to Frost & Sullivan, the total incidence of RAS wild-type mCRC, RM-HNSCC and LA-HNSCC reached 350.1 thousand in 2022 in China and is expected to reach 422.0 thousand by 2030. In 2018, cetuximab was included in the NRDL through price negotiation with a price of RMB1,295 for a 100 mg (20 ml) vial set. According to Frost & Sullivan, the treatment cost for cetuximab was RMB137.8 thousand in 2022.

Clinical trials combining cetuximab with chemotherapy or radiotherapy have demonstrated marked synergy with significant improvement in anti-tumor activity compared to chemo or radiotherapy alone. For mCRC patients with wild-type Kirsten RAS, an oncogene, adding cetuximab to FOLFIRI chemotherapy significantly improved the ORR from 38.6% to 66.3% and extended the median OS from 20.2 months to 28.4 months compared with FOLFIRI alone. For patients with locally advanced HNSCC, cetuximab plus radiation therapy significantly improved the median OS from 29.3 months to 49.0 months compared to radiation alone. Combining cetuximab with platinum-based chemotherapy for the treatment of RM-HNSCC increased the ORR from 19.5% to 35.6% and prolonged the OS from 7.4 months to 10.1 months compared to platinum-based chemotherapy alone. Patients taking cetuximab usually tolerate the drug well. The most common side effects are skin rashes, low magnesium levels in the blood and allergic reactions due to IV infusion.

Mechanism of Action

In normal cells, upon the binding of its growth factor ligands, EGFR initiates a series of signaling events, including the activation of RAS family proteins that subsequently activate gene programs responsible for promoting various cell functions, including proliferation, survival, differentiation, and migration. Tumor cells frequently hijack this signaling pathway by overexpressing EGFR, leading to constant activation that fuels tumor cell growth, invasion, and metastasis. Since EGFR is a major oncogenic driver in many cancers, it has become one of the most attractive targets for anti-cancer treatments, with EGFR mAbs being one of the major therapeutic approaches. EGFR mAbs have been shown to be effective against tumors with wild-type RAS gene.

A140 is an EGFR mAb that exerts its anti-tumor effects via several mechanisms. By binding to the extracellular domain of EGFR, A140 blocks ligand binding to the receptor, thereby inhibiting ligand-dependent activation of EGFR and its downstream oncogenic signaling. A140 also downregulates the expression of EGFR by promoting its internalization, a process where EGFR is engulfed within the cell and ultimately degraded. These inhibitory functions induce cell cycle arrest to halt the progression of tumor cell division, decrease the expression of pro-angiogenic factors to suppress tumor cell invasion and metastasis, as well as promote apoptosis, or programmed cell death, in tumor cells by altering the balance of pro/anti-apoptosis factors. In addition to interrupting EGFR signaling, A140 can trigger an immunologic anti-tumor effects such as ADCC), ADCP, CDC and adaptive immunity-mediated by $CD8^+$ cytotoxic T cells in which NK cells, macrophages, complement and cytotoxic T cells can recognize and bind to the tumor cells bound with A140, leading to the activation of cytotoxic signaling that kills the tumor cells.

Market Opportunity and Competition

RAS wild-type mCRC. CRC is the third most common cancer and one of the leading causes of cancer mortality in China. Of all the newly diagnosed CRC patients, approximately 20% have metastatic disease at presentation and about 80% with CRC eventually develop metastases. RAS wild-type mCRC accounts for approximately half of all mCRC cases. According to Frost & Sullivan, the incidence of RAS wild-type mCRC in China increased from 173.7 thousand in 2017 to 202.5 thousand in 2022 and is expected to reach 253.6 thousand in 2030.

In China, the treatment paradigm for RAS wild-type mCRC primarily involves combination chemotherapy with cetuximab or anti-angiogenic mAb bevacizumab. Although either cetuximab or bevacizumab can be used in combination with chemotherapy as the first-line treatment, a retrospective trial analysis published in JAMA Oncology shows that cetuximab in combination with chemotherapy regimen has a better ORR and OS compared with bevacizumab in combination with chemotherapy regimen for treating RAS wild-type mCRC patients with left-sided tumors.

HNSCC. HNSCC is a prevalent and deadly cancer that occurs in the mucous membranes of mouth, nose, and throat. Over 90% of head and neck tumors is HNSCC. LA-HNSCC and RM-HNSCC account for approximately 60% and 50% of all HNSCC cases, respectively. According to Frost & Sullivan, the incidence of LA-HNSCC in China increased from 72.4 thousand in 2017 to 80.5 thousand in 2022 and is forecasted to reach 91.9 thousand in 2030. The incidence of RM-HNSCC in China increased from 60.3 thousand in 2017 to 67.1 thousand in 2022 and is expected to reach 76.6 thousand in 2030.

In China, the current treatment paradigm of LA-HNSCC comprises surgery, radiotherapy, platinum-based chemotherapy and targeted therapy. First-line treatment options include surgery with or without radiotherapy or radiochemotherapy, radiotherapy in combination with platinum-based chemotherapy, and induction chemotherapy followed by radiotherapy, with cetuximab in combination with radiotherapy available in the 2L setting. For RM-HNSCC, PD-1 mAb monotherapy and doublet chemotherapy in combination with cetuximab represent the first-line treatment options, with PD-1 inhibitor nivolumab as monotherapy in the 2L setting. Compared with PD-1 mAb Keytruda as a monotherapy, doublet chemotherapy in combination with cetuximab demonstrated greater therapeutic benefits in terms of median PFS (5.0 months with cetuximab plus chemotherapy, 3.2 months with Keytruda) and ORR (35.0% with cetuximab plus chemotherapy, 19.0% with Keytruda).

Despite the competition, the demand for cetuximab is increasing, especially after it was included in the NRDL in 2018. However, cetuximab still commands a high cost with approximately RMB11,000 per month in 2022. The high cost of cetuximab posts substantial financial burdens on patients and health insurance providers, indicating a substantial unmet need for cetuximab biosimilars to improve drug affordability. Although a number of biotech companies in China are developing cetuximab biosimilars, none had been approved as of the Latest Practicable Date. As of the Latest Practicable Date, there were six cetuximab biosimilar candidates in phase 1 or beyond in China, with three of them in phase 3. For details, see "Industry Overview – China's EGFR mAb Market – Competitive Landscape of EGFR mAbs."

Summary of Clinical Trial Data

Following CDE's guidelines, we initiated a phase 1 clinical trial in China in January 2017 to demonstrate PK bioequivalence of A140 to cetuximab and completed this trial in September 2017. As phase 2 trial is not required for biosimilars, we commenced a pivotal phase 3 clinical trial in China in December 2020. Set forth below is a summary of the key data from A140's completed and ongoing clinical trials.

Pivotal Phase 3 Clinical Trial for RAS wild-type mCRC in combination with mFOLFOX6

This is a double-blind, randomized, multi-center head-to-head trial to evaluate A140's efficacy and safety versus cetuximab as a 1L treatment in combination with mFOLFOX6 chemotherapy regimen for treating RAS wild-type mCRC. This trial plans to enroll 686 subjects in about 80 clinical research centers in China.

Trial Objectives. The primary endpoint is the study drugs' ORR by week 16 in accordance with RECIST 1.1. The secondary endpoints include ORR by week 16 assessed by trial investigators, DCR, DOR, PFS, OS, safety of A140 and cetuximab and the correlation between ADA and plasma concentration of the study drugs.

Trial Progress. As of the Latest Practicable Date, this trial was ongoing with patient enrollment completed in November 2022.

Trial Design. The trial consists of two stages, the double-blind stage and the single-arm stage. In the double-blind stage, subjects are randomized 1:1 to receive mFOLFOX6 plus either A140 or cetuximab at 400 mg/m^2 for 2 hours ± 10 minutes for the first week and 250 mg/m^2 weekly maintenance for subsequent weeks. In the single-arm stage, the subjects who have benefitted from double-blind study treatment as adjudicated by trial investigators continue to receive A140-mFOLFOX6 treatment until disease progression, intolerable toxicity, or patient/investigator's decision to withdraw.

Phase 1 Clinical Trial in Chinese Healthy Subjects

This was a single-center, double-blind and randomized trial to evaluate the similarity of PK profiles of A140 and cetuximab among Chinese healthy males. This trial was conducted in 82 subjects in one clinical research center in China.

Trial Objectives. The primary endpoint was A140's AUC from drug administration to the end of the dosing period (AUC_{0-t}), a PK parameter that describes the observed drug exposure. The secondary endpoints were additional PK parameters, as well as safety and immunogenicity of A140.

Trial Progress. This trial was completed in September 2017.

Trial Design. Subjects were enrolled for 6 months and divided into 2 cohorts. 41 subjects received 250 mg/m^2 of A140 (2 mg/ml) and 41 subjects received 250 mg/m^2 of cetuximab (5 mg/ml) for two hours.

PK Data. A140 demonstrated PK bioequivalence to cetuximab, as demonstrated in the table below that the 90% confidential intervals (CIs) for the geometric mean ratios of three PK measures, AUC_{0-t}, $AUC_{0-\infty}$ and C_{max}, of each cohort fell within the 80%~125% equivalence margin, as set forth in the "Technical Guidelines for Human Bioequivalence Study of Chemical Drug Biosimilar with Pharmacokinetic Parameters as Endpoint Evaluation Indicators 《以藥動學參數為終點評價指標的化學藥物仿製藥人體生物等效性研究技術指導原則》)" issued by the NMPA.

	Geometric mean and ratio				
Pharmacokinetic parameters (unit)	**A140**	**Cetuximab**	**(A140/ Cetuximab) %**	**CV (coefficient of variation) %**	**90% CI**
C_{max} (μg/ml)[1]	158.49	169.82	95%	13.59%	89%~100%
AUC_{0-t} (hr*μg/ml)[2]	11,220.18	10,715.19	105%	18.86%	98%~112%
$AUC_{0-\infty}$ (hr*μg/ml)[3]	11,220.18	10,964.78	105%	18.64%	98%~112%

Notes:

(1) Cmax: maximum drug concentration in plasma;

(2) AUC_{0-t}: AUC from drug administration to the end of the dosing period;

(3) $AUC_{0-\infty}$: AUC from drug administration to the time that the drug is no longer present in the subject's body.

Safety Data. There was no observable difference in safety profiles between A140 and cetuximab.

Immunogenicity Data. A140 demonstrated an immunogenicity profile similar to that of cetuximab. The incidence of ADA formulation was detected as 7.5% in both cohorts, of which the PK features show no obvious difference among ADA-positive and ADA-negative subjects.

Conclusion. A140 demonstrated PK bioequivalence and a similar safety and immunogenicity profile to cetuximab.

Next Steps

We expect to complete our pivotal phase 3 clinical trial of A140 in China in the second half of 2023 and file an NDA with the NMPA for RAS wild-type mCRC in the second half of 2023. Further, we will follow the CDE's "Technical Guidelines for Similarity Evaluation and Indication Extrapolation of Biosimilars" (《生物類似藥相似性評價和適應症外推技術指導原則》) to explore the opportunities of A140 for treating other indications for which cetuximab has been already approved, including RM-HNSCC and LA-HNSCC, as well as indications for which cetuximab is currently under clinical development in China, such as NSCLC and cSCC.

A140 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

A400 – A Second-generation Selective RET Inhibitor

Overview

A400 is positioned to be the first domestically developed second-generation selective RET inhibitor for treating RET+ solid tumors in China. RET alterations have been reported to be a major oncogenic driver in about 2% of all cancers, most notably in NSCLC and MTC. Although two first-generation selective RET inhibitors were approved in China for RET+ solid tumors as of the Latest Practicable Date, their therapeutic benefits are limited, in part, by acquired RET drug-resistant mutations and safety issues such as hypertension and hematological toxicity, underscoring the need for novel selective RET inhibitors with improved safety and better efficacy against drug resistant mutations. A400 is designed with a novel proprietary molecular structure to address selective RET inhibitor resistance while maintaining target selectivity, efficacy and safety with reduced manufacturing cost and difficulty. Building upon its strong potency against diverse RET alterations and CNS penetration demonstrated in preclinical studies, A400 showed promising anti-tumor efficacy in patients with advanced RET+ solid tumors, highlighted by ORR of 74% and 66.7% at RP2D for first-line and 2L+ advanced RET+ NSCLC, respectively, based on preliminary results from its ongoing phase 1/2

trial. Notably, A400 also demonstrated therapeutic potential in selective RET inhibitor-resistant patients with an ORR of 33% and DCR of 83% at RP2D, as well as a differentiated safety profile, with no incidence of grade 3 or above lymphopenia and thrombocytopenia and substantially lower incidence of grade 3 or above cardiovascular AEs (e.g., hypertension), hematological toxicity and electrolyte abnormalities, based on non-head-to-head cross-trial comparisons with approved selective RET inhibitors. These encouraging results support the potential of A400 to be an efficacious and safe second-generation selective RET inhibitor for NSCLC, MTC and other solid tumors with a high prevalence of RET alterations.

We are rapidly progressing the clinical development of A400 in China. We completed the dose escalation study of a phase 1/2 trial for advanced RET+ solid tumors with ongoing patient enrollment for the dose expansion study. Based on the promising preliminary results of A400 in both first-line and 2L+ advanced RET+ NSCLC patients, we completed CDE clinical consultation and initiated a pivotal trial for 2L+ advanced RET+ NSCLC in May 2023. Moreover, we plan to commence a pivotal trial for 1L advanced RET+ NSCLC in the second half of 2023 and a pivotal trial for advanced RET+ MTC in the first half of 2024. For details, see "– Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A400 – Clinical Development Plan."

Mechanism of Action

The RET gene is a proto-oncogene, a gene that promotes cancer formation when altered by mutations or rearrangements. In normal conditions, it encodes the RET transmembrane receptor tyrosine kinase, an enzyme-linked receptor that exists across a cell membrane with important functions in organ development. However, gene mutations and fusions that occur on the RET gene can result in a mutant RET protein that becomes active in the absence of a ligand. Mutant RET drives the hyperactivation of downstream signalling pathways, leading to uncontrollable cell growth and tumor formation. Given the key role of altered RET in driving cancer development, RET-targeting therapies have been a promising approach to treat RET+ cancers.

A400 is engineered to provide specific RET pathway inhibition with potentially greater efficacy, through comprehensive analysis of the key chemical groups and clinical manifestations of first-generation selective RET inhibitors Gavreto (pralsetinib) and Retevmo (selpercatinib), the only two FDA and NMPA-approved selective RET inhibitors as of the Latest Practicable Date. It possesses nanomolar potency against diverse RET alterations, including certain mutations that mediate resistance to existing selective RET inhibitors. A400's binding to RET suppresses RET's enzymatic activity in RET+ cancers, thereby interrupting RET-mediated oncogenic signal. The pharmacological properties of A400 were also optimized to facilitate CNS penetration, which potentially allows A400 to effectively treat brain metastases, a common complication of RET+ solid tumors.

Market Opportunity and Competition

RET alterations have been found in about 2% of cancers, most prominently in NSCLC and MTC, the first two indications that A400 is designed to target.

RET+ NSCLC. NSCLC accounts for over 85% of LC, which is the second most common cancer and the leading cause of cancer death globally. RET+ NSCLC amounts to approximately 1-2% of total NSCLC cases. According to Frost & Sullivan, the incidence of RET+ NSCLC in China grew from 13.6 thousand in 2017 to 15.9 thousand in 2022 and is expected to reach 20.0 thousand in 2030.

In China, the first-line treatment options largely follow treatment guidelines recommended for driver mutation-negative advanced NSCLC, which involves chemoimmunotherapy with or without anti-angiogenic mAb bevacizumab and monotherapy with PD-L1 inhibitor for PD-L1+ patients, with the addition of first-generation selective RET inhibitor Retevmo as another first-line option. The 2L+ treatment options include single-agent chemotherapy, doublet chemotherapy with or without bevacizumab, PD-1 inhibitor monotherapy, and first-generation selective RET inhibitors Gavreto and Retevmo (for patients who have not received first-line targeted therapy).

Although both first-generation selective RET inhibitors demonstrated robust initial treatment responses, their therapeutic benefits are limited by RET drug-resistant mutations acquired during the treatment course, as well as safety issues such as hypertension and hematological toxicity, necessitating the development of novel selective RET inhibitors with improved safety and better efficacy against mutations that confer selective RET inhibitor resistance. As of the Latest Practicable Date, according to Frost & Sullivan, Gavreto and Retevmo were the only selective RET inhibitors approved for the treatment of advanced RET+ NSCLC in China, and there were four selective RET inhibitor candidates in phase 1/2 or beyond for RET+ NSCLC in China. For details regarding the competitive landscape of selective RET inhibitors in China, see "Industry Overview – China's Selective RET Inhibitor Market – Competitive Landscape of Selective RET Inhibitors."

RET+ MTC. TC is the most common type of endocrine cancers. According to studies published in *The Lancet Diabetes & Endocrinology*, it was the fastest growing cancer in China in recent years. MTC accounts for approximately 3% of total TC cases. RET mutations represent a major driver of MTC, occurring in about 90% of MTCs, and are associated with advanced disease and worse clinical outcome. According to Frost & Sullivan, the incidence of RET+ MTC in China increased from 5.6 thousand in 2017 to 6.2 thousand in 2022 and is expected to increase to 7.4 thousand in 2030.

The standard treatments for advanced MTC in China include Gavreto in the first-line setting and Retevmo in the 2L setting.

Despite the initially promising treatment responses to Gavreto and Retevmo, many patients eventually progress as their tumors acquire RET mutations that confer resistance to these two RET inhibitors. Moreover, Retevmo and Gavreto are associated with safety issues such as hypertension and hematological toxicity that limit their clinical use. This indicates a significant unmet need for novel selective RET inhibitors with improved safety and better efficacy against RET drug-resistant mutations that confer selective RET inhibitor resistance. As of the Latest Practicable Date, according to Frost & Sullivan, Gavreto and Retevmo were the only selective RET inhibitors approved for the treatment of advanced RET+ MTC in China, and there were three selective RET inhibitor candidates in phase 1/2 or beyond for advanced RET+ MTC in China. For details regarding the competitive landscape of selective RET inhibitors in China, see "Industry Overview – China's Selective RET Inhibitor Market – Competitive Landscape of Selective RET Inhibitors."

Competitive Advantages

Promising Anti-tumor Efficacy with potential to overcome first-generation selective RET inhibitor resistance. Based on preliminary clinical data from its phase 1/2 trial, A400 demonstrated promising efficacy in patients with advanced RET+ solid tumors, highlighted by ORR of 74% and 66.7% at RP2D (90 mg) for 1L and 2L+ advanced RET+ NSCLC, respectively. According to the latest non-head-to-head data publicly available, the preliminary ORRs demonstrated by A400 against advanced RET+ NSCLC in both 1L patients and selective RET inhibitor-naïve 2L+ patients are comparable or better than those of first-generation selective RET inhibitors Gavreto and Retevmo, as illustrated in the diagram below.

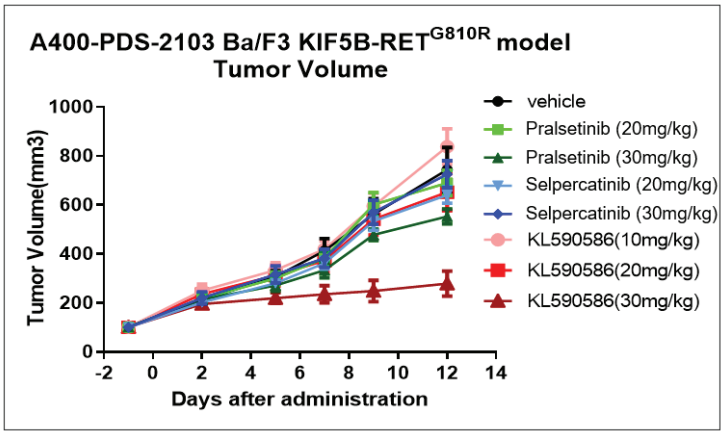
Drug name (Dosage)	**A400 (90 mg QD)**				**Gavreto (400 mg QD)**		**Retevmo (160 mg BID)**	
Patient group	1L	2L+			1L	2L+	1L	2L+
		SRI-naïve	SRI-resistant	Overall		SRI-naïve		SRI-naïve
Patient number	19	15	6	21	27	87	39	105
ORR	74%	80%	33%	66.7%	70%	57%	85%	64%
DCR	100%	93%	83%	90.5%	85%	91%	95%	93%

Note:

(1) SRI refers to selective RET inhibitor.

Sources: Gavreto: Gavreto's drug label; Retevmo: Retevmo's drug label

Notably, designed with a novel proprietary molecular structure to address selective RET inhibitor resistance, A400 demonstrated promising clinical efficacy in selective RET inhibitor-resistant patients, including seven patients (six RET+ NSCLC, one RET+ MTC) who had prior first-generation selective RET inhibitor Gavreto, with an ORR of 33% and a DCR of 83% at RP2D, based on preliminary clinical data from its phase 1/2 trial. These encouraging results are consistent with the findings from our head-to-head preclinical studies. As demonstrated in the diagram below, A400 demonstrated greater TGI in an *in vivo* drug-resistant (RET G810R mutation) xenograft model, compared with Gavreto (pralsetinib) and Retevmo (selpercatinib) at the same dose. Altogether, these clinical and preclinical results support the promising anti-tumor efficacy potential of A400 for treating 1L, 2L+ and selective RET inhibitor-resistant patients with advanced RET+ solid tumor.



Differentiated Safety Profile. A400 showed a differentiated safety profile based on preliminary results from its phase 1/2 trial, where most reported AEs were mild or moderate. As shown in the table below, compared with the two approved first-generation selective RET inhibitors, A400 demonstrated no incidence of grade 3 or above lymphopenia and thrombocytopenia and substantially lower incidence of grade 3 or above cardiovascular AEs (e.g., hypertension), hematological toxicity and electrolyte abnormalities. Although no head-to-head data are available at this stage, we believe these comparisons below indicate the differentiated features and advantages of A400 from a safety perspective.

Grade 3 or above TRAEs for A400, Retevmo and Gavreto[(1)]

Preferred term	A400 90 mg QD (N=53)	Retevmo 160 mg BID (N=796)	Gavreto 400 mg QD (N=220)
		Incidence (%)	
Elevated AST level	1.1	11	2.3
Elevated ALT level	1.1	12	2.3
Anemia	0	3.5	9
Hypocalcemia	0	5.7	1.8
Lymphopenia	0	20	19
Hyponatremia	0	11	7
Phosphate reduction	0	N/A	11
Neutropenia	0	3.2	16
Diarrhea	0	5	3.2
Hypertension	0	20	14
Infectious Pneumonia	1.1	N/A	8

Note:

(1) This table summarizes the grade 3 or above TRAEs with an incidence of ≥ 5% for A400, Retevmo, or Gavreto.

Sources: Gavreto: Gavreto's drug label; Retevmo: Retevmo's drug label

Clinical Development Plan

We are rapidly progressing the clinical development of A400 in China. Following A400's IND approval in June 2021, we initiated a phase 1/2 clinical trial in patients with advanced RET+ solid tumors in July 2021.

Based on the promising preliminary results of A400 in 1L and 2L+ advanced RET+ NSCLC patients, we completed CDE clinical consultation and initiated a pivotal trial for 2L+ advanced RET+ NSCLC in May 2023. We expect to commence a pivotal trial for 1L advanced RET+ NSCLC in the second half of 2023. Moreover, we plan to initiate a pivotal trial in the first half of 2024 to advance the development of A400 for advanced RET+ MTC.

The table below sets forth our clinical development plan for A400:

Indication (Lines of Treatment)	Trial phase	Trial status	(Expected) Trial start date	Expected trial end date	Location
Advanced RET+ NSCLC (1L)	Pivotal	CDE clinical consultation completed	(2H 2023)	2H 2026	China
Advanced RET+ NSCLC (2L+)	Pivotal	Ongoing	May 2023	1H 2026	China
Advanced RET+ MTC	Pivotal	In planning	(1H 2024)	1H 2027	China
Adjuvant or neoadjuvant RET+ NSCLC	Phase 2	In planning	Pending	N/A	China
Advanced RET+ solid tumors[(1)]	Phase 1/2	Completed: dose escalation Ongoing: dose expansion	July 2021	1H 2024	China

Note:

(1) Including NSCLC, MTC and other selective RET inhibitor-naïve solid tumors, and selective RET inhibitor-resistant solid tumors.

Summary of Clinical Trial Data

We are evaluating A400 in a phase 1/2 clinical trial for advanced RET+ solid tumors. Set forth below is a summary of the key data from A400's ongoing clinical trial.

Phase 1/2 Clinical Trial for Advanced RET+ Solid Tumors

This is an open-label, multi-center, single-arm phase 1/2 trial to evaluate the safety, tolerability, MTD and RP2D of A400 in patients with advanced RET+ solid tumors. This trial plans to enroll 414 adult subjects.

Trial Objectives. The primary endpoints of phase 1 include the safety and tolerability of A400 in patients with advanced RET+ solid tumors, and to determine the MTD and RP2D. The primary endpoint of phase 2 is the IRC-assessed ORR. The secondary endpoints include the ORR assessed by Investigator Assessment according to RECIST 1.1 or Response Assessment in Neuro-Oncology (RANO), and the DOR, TTR, DCR, PFS, CNS ORR and CNS DOR assessed by the IRC and trial investigators. All efficacy parameters are assessed based on RECIST 1.1 or RANO.

Trial Progress. Dose escalation was completed in November 2022, with 19 patients enrolled and dosed at 10 mg (n=1), 20 mg (n=3), 40 mg (n=3), 60 mg (n=3), 90 mg (n=6) and 120 mg (n=3) once daily. As of December 30, 2022, patient enrollment for the dose expansion cohort was ongoing, with 87 patients enrolled and dosed at 10 mg, 20 mg, 40 mg, 60 mg, 90 mg or 120 mg once daily.

Trial Design. This study is divided into phase 1 and phase 2. Phase 1 was a dose escalation and dose expansion study in which subjects received 10, 20, 40, 60, 90, or 120 mg of oral A400 capsule once daily until disease progression, intolerable toxicity, death, or other treatment termination criteria are met. In phase 2, subjects are assigned into different cohorts based on their respective types of RET+ tumors to receive A400 at RP2D for cycles of 28 days until disease progression, intolerable toxicity, death or other treatment termination criteria are met.

Efficacy Data.

RET+ NSCLC. Clinical responses were observed from 40 mg onwards. As of the data cut-off date (December 30, 2022), 57 patients were evaluable for response assessment. The ORRs and DCRs of the 57 evaluable patients across 40, 60, 90 and 120 mg A400 cohorts are illustrated in the diagram below. In the 4 1L patients with measurable brain metastases, the brain metastasis ORR was 75.0% (3/4) and brain metastasis DCR was 100% (4/4).

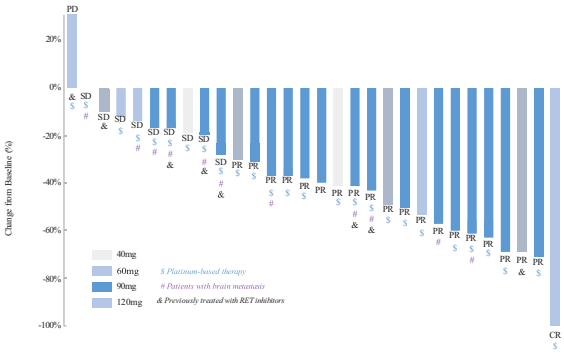
	40 mg			**60 mg**			**90 mg (RP2D)**			**120 mg**			**Overall**		
Patient group	1L	2L+		1L	2L+		1L	2L+		1L	2L+		1L	2L+	
		SRI-naïve	SRI-resistant		SRI-naïve	SRI-resistant		SRI-naïve	SRI-resistant		SRI-naïve	SRI-resistant		SRI-naïve	SRI-resistant
Patient number	0	2	0	4	4	1	19	15	6	2	2	2	25	23	9
ORR	0%	50%	0	100%	50%	0	74%	80%	33%	50%	100%	50%	76%	74%	33%
DCR	0%	100%	0	100%	100%	0	100%	93%	83%	50%	100%	100%	92%	96%	78%

Note:

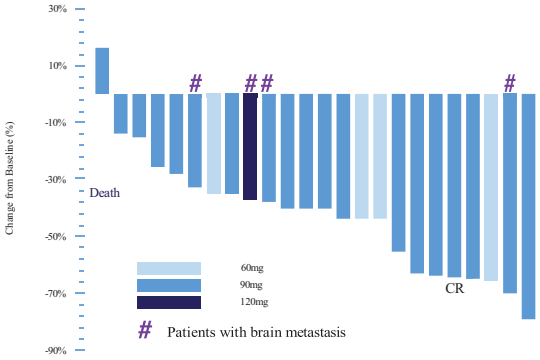
(1) SRI refers to selective RET inhibitor.

The below waterfall plots show the best percentage change from baseline in target lesions for each evaluable patient.

Best percentage change in the diameter sum of target lesions of 2L+ RET+ NSCLC patients from baseline

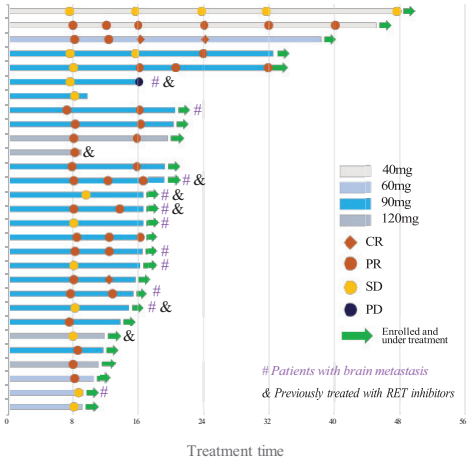


Best percentage change in the diameter sum of target lesions of 1L RET+ NSCLC patients from baseline

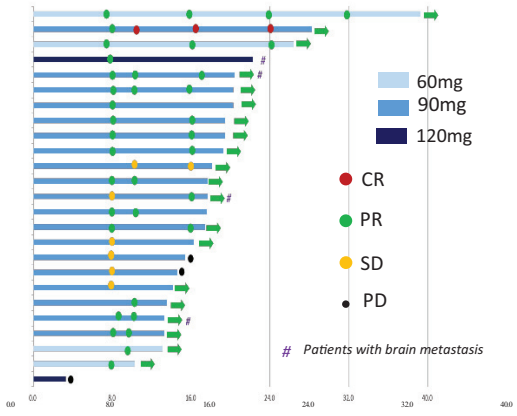


The swimmer plots below show the durable objective responses and disease stabilization of the evaluable patients with SD, PR and CR.

Swimmer plot of 2L+ RET+ NSCLC patients with SD/PR/CR



Swimmer plot of 1L RET+ NSCLC patients



Other RET+ indications. Although the data was not mature, potential efficacy of A400 was observed in patients with advanced RET+ MTC, advanced RET+ PC and advanced RET+ OC.

Safety Data. As of the data cut-off date (December 30, 2022), of 87 patients evaluable for safety assessment, TRAEs were reported in 81 (93.1%) patients. Most TRAEs were grade 1 or 2, and recovered after safety monitoring, dose modification and corresponding treatment. Grade 3 or above TRAEs were reported in 21 (24.1%) patients. The table below summarizes the TRAEs with an incidence of > 15% across the A400 10, 20, 40, 60, 90 and 120 mg cohorts.

Preferred term	A400 (10-20-40-60-90-120mg, QD) (N=87), n (%) All grades (%)	>Grade 3 (%)
At least one TRAE	81 (93.1)	21 (24.1)
Elevated AST level	44 (50.6)	1 (1.1)
Elevated ALT level	42 (48.3)	1 (1.1)
Elevated blood creatinine	29 (33.3)	0
Elevated blood bilirubin	28 (32.2)	0
Constipation	28 (32.2)	0
Headache	27 (31.0)	1 (1.1)
Hypoesthesia	19 (21.8)	0
Elevated blood creatine phosphokinase	18 (20.7)	1 (1.1)
Urinary retention	18 (20.7)	0
Anemia	17 (19.5)	1 (1.1)
Hyperuricemia	17 (19.5)	0
Dizziness	15 (17.2)	1 (1.1)
Blurred vision	15 (17.2)	
Elevated blood alkaline phosphatase	14 (16.1)	2 (2.3)

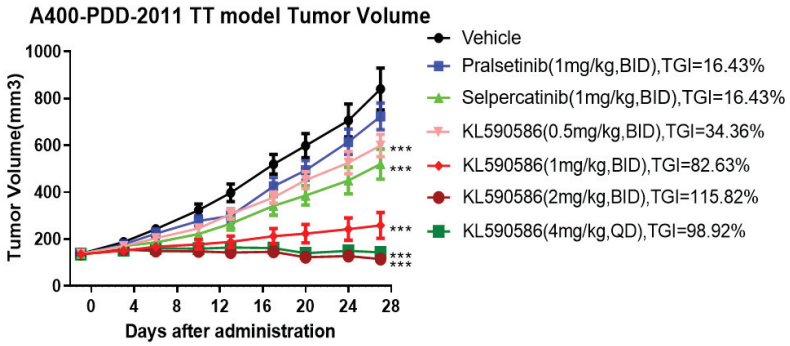
PK Data. Consistent with preclinical findings, A400 exhibited a longer human half-life and higher plasma exposure than Gavreto and Retevmo in non-head-to-head, cross-trial comparisons.

Conclusion. Based on preliminary clinical data, A400 demonstrated a differentiated safety profile and promising anti-tumor activity across a range of advanced RET+ solid tumors with potential for treating brain metastasis and drug-resistant patients.

Summary of Preclinical Data

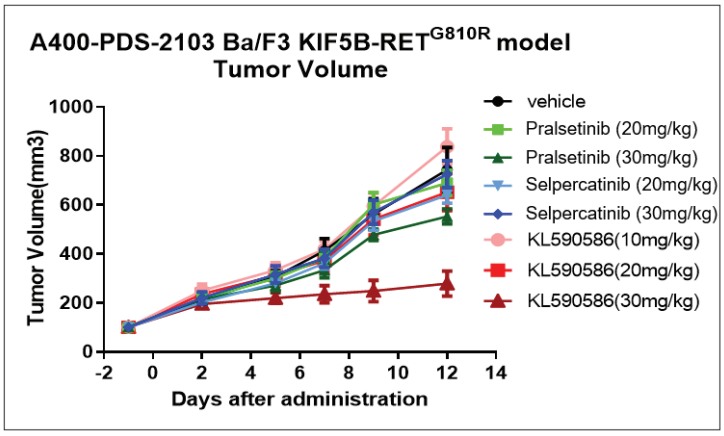
We have conducted a series of *in vitro* and *in vivo* studies to evaluate A400's efficacy, CNS penetration, and potency against drug resistance mutations.

The efficacy of A400, under the drug code of KL590586, was studied in a RET-driven MTC cell line-derived xenograft model with RET^{C634W} mutation, head-to-head against pralsetinib and selpercatinib. As shown in the diagram below, A400 demonstrated a dose-dependent anti-tumor effect, measured by percent of TGI, starting from a dose of 0.5 mg/kg administered twice daily. At the same dose (1 mg/kg), A400 achieved an approximately five-fold and a near two-fold higher TGI than pralsetinib and selpercatinib, respectively, at 28 days after treatment initiation.

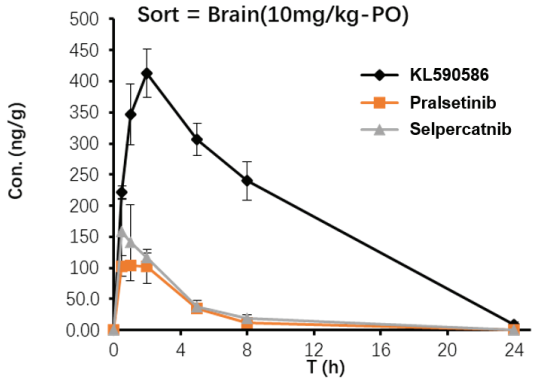


The potency of A400 against drug resistance mutations was assessed in human Ba/F3 cell line engineered to overexpress human KIF5B-RET fusion protein (Ba/F3-KIF5B-RET) that carries G810R/S/C mutations, alongside Gavreto and Retevmo. As shown in the table below, A400 demonstrated a higher potency against G810R/S/C mutations in the Ba/F3-KIF5B-RET cell line than pralsetinib and selpercatinib, indicated by its lower IC_{50} values. In line with this result, A400 demonstrated greater TGI in an *in vivo* drug-resistant (RET G810R mutation) xenograft model, compared with pralsetinib and selpercatinib at the same dose, as demonstrated in the diagram below.

Enzyme Activity – Compound IC_{50} (nM)			
Molecular target	**Pralsetinib**	**Selpercatinib**	**KL590586**
RET^{G810R}	168.45±0.45	73.97±16.40	19.62±0.67
RET^{G810S}	1.77±0.27	5.66±0.22	2.69±0.56
RET^{G810C}	48.81±3.82	151.30±30.70	53.16±10.67
Cell Growth Inhibition Activity – Compound IC_{50} (nM)			
Cell line	**Pralsetinib**	**Selpercatinib**	**KL590586**
Ba/F3-KIF5B-RET^{G810R}	181.50±80.02	116.20±1.15	26.25±5.76
Ba/F3-KIF5B-RET^{G810S}	28.97±4.47	87.89±0.75	20.19±0.35
Ba/F3-KIF5B-RET^{G810C}	146.40±3.40	477.10±4.40	65.35±1.00

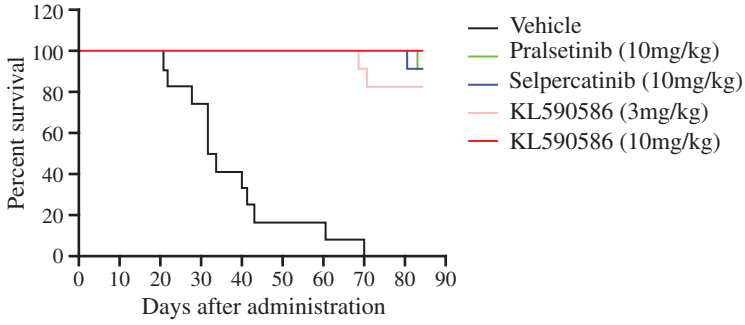


In head-to-head *in vivo* brain penetration studies, A400 exhibited a higher exposure in the brain compared to pralsetinib and selpercatinib, as illustrated below by the concentration-time curves of these three drugs in the brain.



In line with its greater brain penetration, A400 prolonged the survival of intracranial tumor xenograft mice, i.e., a mouse model of brain metastasis using a RET+ cell line derived from human brain metastatic tumors, in head-to-head comparisons with pralsetinib and selpercatinib as illustrated in the diagram below. Together, these results suggest that A400 has a superior brain penetration and efficacy against brain metastasis compared to the two FDA-approved RET inhibitors.

Increased Survival Rate in Intracranial Tumor Xenograft Following KL590586 Treatment



Next Steps

We plan to initiate a pivotal trial for 1L advanced RET+ NSCLC in the second half of 2023 and a pivotal trial in the first half of 2024 for advanced RET+ MTC. For details, see "– Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A400 – Clinical Development Plan."

A400 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

SKB337 – A PD-L1 and CTLA-4 BsAb

SKB337 is a differentiated PD-L1/CTLA-4 bsAb designed to provide dual blockade of PD-L1 and CTLA-4, two clinically validated immune checkpoints for treating solid tumors. Despite their unprecedented effectiveness, the survival benefits offered by existing immune checkpoint inhibitors as monotherapies are only limited to a minority of cancer patients, whereas the increased efficacy of dual immune checkpoint blockade using a PD-1 mAb and a CTLA-4 mAb comes with severe toxicity and substantial treatment cost. Consequently, there is a significant unmet need for novel approaches that can provide effective concurrent blockade of the PD-(L)1 and CTLA-4 pathways with reduced toxicity and better affordability. With the capability to simultaneously target two antigens on different cell types, bsAb-based therapies represent a promising strategy to provide dual immune checkpoint blockade with improved safety, cost-effectiveness and ease of dosing, supported by the recent NMPA approval of the first and only PD-1/CTLA-4 bsAb Kaitanni (cadonilimab) for relapsed or metastatic cervical cancer.

SKB337 is designed to exploit the differences in timing, location and non-overlapping immune-inhibitory effects mediated by CTLA-4 and PD-L1. It potentially invigorates anti-tumor immunity via the following synergistic mechanisms: (i) promote the expansion and migration of activated T cells to the tumor site by blocking CTLA-4 on T cell surface during the priming phase, (ii) relieve T cells from CTLA-4 and PD-(L)1-mediated inhibition by blocking CTLA-4 on regulatory T cells (Tregs) and PD-L1 on tumor cells and immunosuppressive antigen-presenting cells (APCs), and (iii) deplete Tregs via ADCC and antibody-dependent cell-mediated phagocytosis (ADCP), in which NK cells and macrophages, respectively, are induced by the Fc region of SKB337 to eliminate the SKB337-bound Tregs.

As of the Latest Practicable Date, Kaitanni was the only approved PD-(L)1/CTLA-4 bsAb in China. Including SKB337, there were five PD-(L)1/CTLA-4 bsAbs in phase 1 or beyond in China as of the same date.

In light of the risk of immune-related adverse effects historically associated with CTLA-4 blockade, we specifically designed SKB337 to have a higher affinity for PD-L1 compared to CTLA-4. Given that PD-L1 is frequently overexpressed on tumor cells and immunosuppressive cells in the tumor microenvironment, our differentiated design potentially enriches SKB337 in the tumor site and reduces off-tumor toxicity associated with CTLA-4 blockade.

We received IND approval in February 2021 from the NMPA. We are evaluating SKB337 in a phase 1 dose escalation trial in patients with advanced solid tumors in China, which we initiated in May 2021 and expect to complete in the second half of 2023.

SKB337 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

A289 – A LAG-3 mAb

A289 is a LAG-3 mAb designed to inhibit LAG-3, a new-generation immune checkpoint receptor used by tumor cells to evade immune attacks, for treating solid tumors. To date, the majority of approved immune checkpoint inhibitors target the PD-(L)1 checkpoint. While these PD-(L)1 inhibitors have been paradigm-shifting in various cancer indications, drug resistance limits treatment benefits to only a fraction of cancer patients. Consequently, there is a substantial unmet need for novel inhibitors that target alternative immune checkpoints. LAG-3 is an immune checkpoint receptor highly expressed in various types of immune cells. Based on published studies, it is closely associated with the tumor microenvironment and synergizes with PD-1 in inhibiting anti-tumor immune response. Consequently, LAG-3 has become a foremost target for developing novel single-agent and combination immunotherapy, with its therapeutic potential supported by the recent FDA approval of Opdualag (relatlimab), the first and only FDA-approved LAG-3 inhibitor to date, for treating metastatic melanoma in combination with a PD-1 inhibitor.

For details regarding the incidence of solid tumors in China, see "– Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – SKB337." As of the Latest Practicable Date, there were no anti-LAG-3 drugs approved in China. According to Frost & Sullivan, there were 15 anti-LAG-3 therapies, either as a single agent or in combination with PD-1 mAb or chemotherapy, in phase 1 or beyond in China as of the Latest Practicable Date, with ten LAG-3 mAbs, four LAG-3/PD-(L)1 bsAbs and one LAG-3/TIGIT bsAb. As of the same date, most anti-LAG-3 drug candidates, including A289, were in phase 1 or phase 2 stage.

Leveraging our extensive mAb platform, the development of A289 underwent an extensive antibody screening and optimization process that led to the identification of a novel human LAG-3 mAb with favorable antigen affinity, antigen specificity and thermal stability compared to relatlimab. Further, we also introduced specific mutations (L234A, L235A and G237A) into the antibody heavy chain to abolish cytotoxic ADCC and CDC functions, thereby reducing the potential of A289 to cause unwanted immune-mediated side effects.

We received IND approval from the NMPA in August 2020 and are conducting a phase 1a/1b clinical trial to evaluate A289 in patients with advanced solid tumors in China, which we initiated in May 2021 and expect to complete in the first half of 2023.

A289 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

A296 – A Novel Second-generation Small Molecule STING Agonist

A296 is a novel second-generation small molecule STING agonist designed with a novel non-CDN hybrid bimolecular structure for treating solid tumors. Currently, immunotherapy relies primarily on immune checkpoint inhibition, which has limited effects on cold tumors, i.e., tumors with inadequate preexisting anti-tumor immunity, signifying a significant unmet need for novel immunotherapy to turn cold tumors hot.

STING is a pattern recognition receptor with a central role in activating immunity by mediating a pro-inflammatory type-I interferon (IFN-I) response. It can be activated in response to DNA in the form of cyclic dinucleotides (CDNs), which are compounds comprised of two nucleotides connected to form a ring structure. Multiple published preclinical studies have shown that STING agonists can potentiate immunotherapy efficacy when used in combination with immune checkpoint inhibitors, indicating the potential of STING agonists as a novel immunotherapy strategy.

For details regarding the incidence of solid tumors in China, see "– Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – SKB337." As of the Latest Practicable Date, according to Frost & Sullivan, there were no STING agonists approved worldwide. Including A296, there were four STING agonists in phase 1 or beyond in China as of the Latest Practicable Date, all of which were in phase 1. The first-generation STING agonists that entered clinical stage are in the form of CDNs, which are unstable and thus require intratumoral injection that severely limit their clinical applicability.

To address this shortcoming, we designed A296 with a novel non-CDN hybrid bimolecular structure to improve drug activity, stability and solubility. These improved properties of A296 potentially lead to durable STING activation and allow effective drug administration via IV and intratumoral routes, thus potentially increasing applicability.

We received IND approvals from the NMPA in January and June 2022 separately for a phase 1a trial (administration via IV infusion) and a phase 1 trial (administration via intratumoral injection) to evaluate A296 for IV injection and intratumoral injection, respectively, in advanced solid tumor patients. We initiated the phase 1a trial and the phase 1 trial in April and July 2022, respectively both in China. We expect to complete the phase 1a trial in the first half of 2025 and the phase 1 trial in the first half of 2026.

A296 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

Non-Oncology Franchise

A223 – A JAK1/2 Inhibitor

Overview

A223 is potentially one of the first domestically developed small molecule JAK1/2 inhibitors for multiple autoimmune diseases with large patient populations in China, such as RA and AA. RA is a prevalent autoimmune disease that requires long-term treatment. Inhibiting JAKs is a clinically validated approach for treating RA, with three JAK inhibitors, each with a different selectivity to the four JAKs, approved by the NMPA in China for treating RA. Among them, JAK1/2 inhibitor Olumiant has been demonstrated to better improve the symptoms of RA patients based on cross-trial comparisons of clinical trials of the combination treatment with methotrexate (MTX) for treating RA. However, the approved JAK inhibitors have major safety issues, with black box warning issued by the FDA for increased risks of serious side effects including serious infection, death, malignancy, thrombosis, and major adverse cardiovascular events. Configured with a structural design that retains target selectivity with optimized pharmacological properties, A223 has demonstrated an encouraging safety profile in three completed trials and two ongoing trials, where most TEAEs were mild or moderate with no incidence of black box warning-related safety issues commonly reported by approved JAK inhibitors. Based on preliminary clinical data from its phase 2 trial, A223 demonstrated promising anti-rheumatic efficacy in moderate-to-severe RA patients, with A223 2 mg achieving substantial and statistically significant ACR20 difference of 35.1% (63.6% vs. 28.6%) and ACR50 difference of 33.7% (39.4% vs. 5.7%) at week 12 compared with placebo. Notably, based on non-head-to-head comparison, the ACR20 and ACR50 differences achieved by A223 2 mg are greater than those of Olumiant 4 mg, the approved dosage of Olumiant in China, in Chinese patients with moderate-to-severe RA (ACR20 difference vs. placebo: 30.8%; ACR50 difference vs. placebo: 20.7%). These promising clinical results indicates the potential of A223 to be an effective treatment option with improved efficacy and safety for RA.

Based on the promising preliminary results from A223's ongoing phase 2 trial, we plan to commence a pivotal phase 3 trial in patients with moderate-to-severe RA in China in the second half of 2023. We have also expanded A223's target indication to AA, a common autoimmune disease of the hair follicle, with Olumiant being the first and only systemic treatment approved by the FDA for severe AA and one of the only two disease-specific treatments for the same indication approved in China as of the Latest Practicable Date. We initiated a phase 2 trial for severe AA in China in August 2022, for which we expect to complete patient enrollment in the second half of 2023.

Mechanism of Action

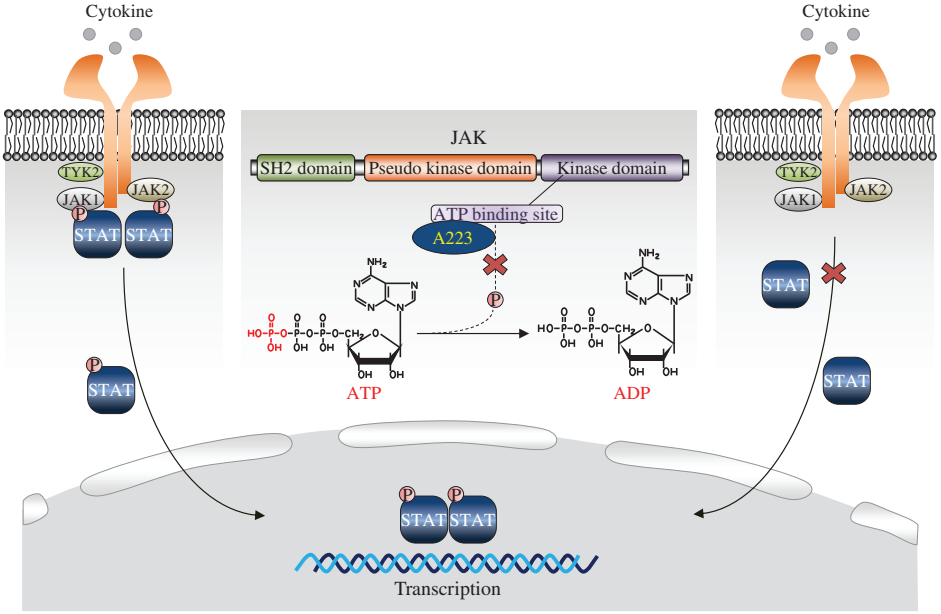
A223 is a small molecule that selectively inhibits two major types of JAKs, JAK1 and JAK2. The JAK-signal transducers and activators of transcription (STAT) pathway is a key signaling route through which cytokines transduce extracellular signals to induce inflammation, control immune response, and orchestrate hematopoiesis, the process through which our body manufactures blood cells. JAKs are a group of four enzymes associated with cytokine receptors and become activated upon cytokine exposure. Via their enzymatic activities, activated JAKs recruit and activate downstream signaling molecules STATs, which drive cytokine-responsive gene expression programs in the nucleus.

RA is a chronic autoimmune disease characterized by systemic inflammation and subsequent progressive destruction of joints. Continuous activation of the JAK-STAT pathway by proinflammatory cytokines leads to the abnormal stimulation of the innate and adaptive immune system, causing persistent joint inflammation that damages joint tissues.

AA is a T cell-mediated autoimmune disease of the hair follicle that ranges in presentation from circular patches on the scalp to complete hair loss. Although the etiology of AA is not completely understood, the pathogenesis of AA is associated with the overexpression of proinflammatory cytokines that signal through the JAK/STAT pathway. This consequently causes cytotoxic T cells to attack hair follicles, resulting in hair loss.

Because of their critical role in mediating the signals from multiple cytokines involved in the pathogenesis of many immune-mediated disorders, JAKs have become attractive targets for treating diverse autoimmune diseases such as RA and AA.

Mechanistically, A223 competes with adenosine triphosphate (ATP) for the ATP-binding site of JAK1/2. Since the enzymatic activity of JAK1/2 requires ATP, the binding of A223 inhibits the activity of JAK1/2. This interrupts JAK-STAT signaling, thereby suppressing cytokine-mediated inflammation and preventing the progression of joint damage in RA and hair follicle damage in AA. The diagram below illustrates the mechanism of action of A223.



Market Opportunity and Competition

RA. RA is a prevalent chronic systemic autoimmune disease in which joints are inflamed, resulting in swelling and pain. As the disease progresses, gradual bone erosion and joint destruction may occur, significantly compromising the quality of life of patients. According to Frost & Sullivan, the prevalence of RA in China increased from 5.8 million in 2017 to 6.0 million in 2022 and are forecasted to reach 6.2 million in 2030.

There is currently no cure for RA. The management of RA in China aims to achieve low disease activity or remission and to control joint damage and pain via the long-term use of disease-modifying anti-rheumatic drugs (DMARDs).

Compared to biologic DMARDs (bDMARDs) that target individual cytokines, JAK inhibitors can simultaneously interrupt the downstream signaling of multiple cytokines, which potentially underlies their effectiveness in RA patients who have failed multiple csDMARDs/bDMARDs therapies. Moreover, bDMARDs are large proteins that may cause immunogenicity, i.e., evoking an undesirable immune response, and require either intravenous infusion or subcutaneous injection for dosing. Conversely, JAK inhibitors are small molecules that are non-immunogenic and can be administered orally, thus potentially improving ease of dosing and treatment compliance.

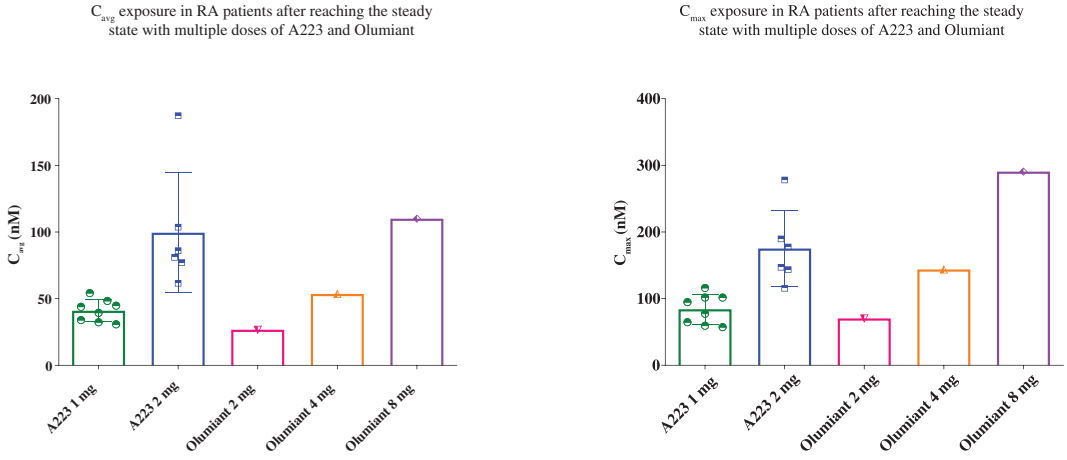
According to Frost & Sullivan, as of the Latest Practicable Date, there were three JAK inhibitors (Xeljanz (tofacitinib), Olumiant (baricitinib) and Rinvoq (upadacitinib)), each with a different selectivity to the four JAKs, approved by the NMPA in China for treating RA. Among them, JAK1/2 inhibitor Olumiant has been demonstrated to better improve the symptoms of RA patients based on cross-trial comparisons of clinical trials of the combination treatment with methotrexate (MTX) for treating RA. In a head-to-head clinical trial for RA, Olumiant was also found to be more efficacious than Xeljanz with a comparable safety profile. These suggest Olumiant may have a better therapeutic potential than JAK inhibitors with other JAK specificities. However, the approved JAK inhibitors have major safety issues, with black box warning issued by the FDA for increased risks of serious side effects including serious infection, death, malignancy, thrombosis, and major adverse cardiovascular events. This underscores a significant unmet need for novel JAK inhibitors with improved safety profile. As of the Latest Practicable Date, according to Frost & Sullivan, there were seven JAK inhibitors in phase 2 or beyond in China for RA. For further details, see "Industry Overview – China's JAK Inhibitor Market – Competitive Landscape of JAK Inhibitors."

AA. AA is a common, distressing autoimmune disease in which immune cells in the body attack hair follicles, causing hair loss. According to Frost & Sullivan, the prevalence of AA in China rose from 3.5 million in 2017 to 4.0 million in 2022 and is projected to rise to 4.5 million in 2030.

Currently, treatment options for AA are limited in China with only Minoxidil, a potassium channel opener, and Olumiant approved as the only disease-specific treatments for severe AA. Inhibiting JAK1/2 represents a clinically proven strategy for AA, underlined by the FDA approval of Olumiant as the first and only systemic treatment for severe AA and its recent NMPA approval for the same indication. As of the Latest Practicable Date, according to Frost & Sullivan, there were four JAK inhibitors in phase 2 or beyond in China for AA. For further details, see "Industry Overview – China's JAK Inhibitor Market – Competitive Landscape of JAK Inhibitors."

Competitive Advantages

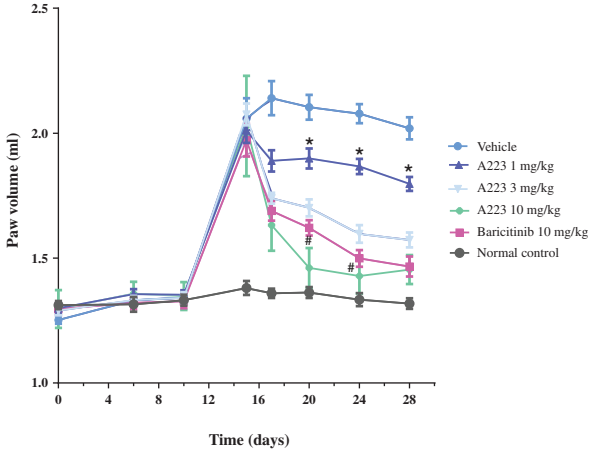
Potentially Lower Effective Dose. A223 is configured with a structural design that retains target selectivity with optimized pharmacological properties. In its phase 1b trial in RA patients, A223 at 2 mg demonstrated a comparable level of C_{avg} compared with Olumiant at 8 mg, while the C_{max} of A223 at 2 mg was significantly lower than that of baricitinib at 8 mg, based on non-head-to-head cross-trial comparison as shown in the diagram below.



Sources:

Olumiant: Olumiant's FDA filing documents.

Moreover, in a head-to-head collagen-induced arthritis (CIA) rat model, a widely used *in vivo* model to mimic joint inflammatory symptoms in RA, CIA rat treated with A223 at 3 mg/kg showed a comparable reduction of paw swelling (an indicator of RA joint inflammation) to that of Olumiant (baricitinib) at 10 mg/kg, while those treated with A223 at 10 mg/kg had a greater paw swelling reduction than baricitinib at the same dose, as shown in the diagram below. This, together with the PK results from A223's phase 1b trial, suggests that A223 may be effective at a lower dose than Olumiant with potentially reduced side effects.



★: A223 1 mg/kg compared with Vehicle, $p < 0.01$
#: A223 10 mg/kg compared with baricitinib, $p < 0.05$

Promising Anti-rheumatic Efficacy. Based on preliminary clinical data from its phase 2 trial, A223 demonstrated dose-dependent ACR20 responses in moderate-to-severe RA patients. A223 1 mg and 2 mg achieved substantial and statistically significant ACR20 differences of 31.4% (60.0% vs. 28.6%) and 35.1% (63.6% vs. 28.6%), respectively, at week 12 compared with placebo. Moreover, A223 2 mg also achieved substantial and statistically significant ACR50 differences of 33.7% (39.4% vs. 5.7%), at week 12 compared with placebo.

Notably, as shown in the table below, the ACR20 and ACR50 differences (vs. placebo) achieved by A223 2 mg are greater than those of Olumiant 4 mg, the approved dosage of Olumiant in China, in Chinese patients with moderate-to-severe RA (ACR20 difference vs. placebo: 30.8%; ACR50 difference vs. placebo: 20.7%), based on non-head-to-head cross-trial comparison. These promising clinical results indicates the potential of A223 to be an effective treatment option with improved efficacy and safety for RA.

Non-head-to-head comparison of ACR20 and ACR50 differences (treatment vs. placebo) of A223 and Olumiant

	Treatment ACR20 *(%)*	**Placebo ACR20** *(%)*	**ACR20 difference (treatment vs. placebo)** *(%)*	**Treatment ACR50** *(%)*	**Placebo ACR50** *(%)*	**ACR50 difference (treatment vs. placebo)** *(%)*
A223 1mg	60.0	28.6	31.4	20.0	5.7	14.3
A223 2mg	63.6	28.6	35.1	39.4	5.7	33.7
Olumiant 4mg	53.4	22.6	30.8	25.0	4.3	20.7

Sources: Olumiant: Yang Y, et al. Rheumatol Ther 2020

Encouraging Safety Profile. In line with our PK results, A223 demonstrated encouraging safety profile across three completed trials and two ongoing trials, where most TEAEs were mild or moderate with no incidence of black box warning-related safety issues commonly reported by approved JAK inhibitors. Based on preliminary data from A223's phase 2 trial in moderate-to-severe RA patients, the overall incidence of TEAEs across the A223 treatment cohorts (52.5%) was comparable to that of the placebo cohort (58.5%), with no obvious dose-dependent incidence of TEAEs in the treatment cohorts. Altogether, these results indicate the encouraging safety profile of A223.

Clinical Development Plan

We are rapidly progressing the clinical development of A223 in China. Based on the promising preliminary results from our ongoing phase 2 trial, we plan to initiate a pivotal phase 3 trial of A223 in moderate-to-severe RA patients in China in the second half of 2023. We have also expanded A223's target indication to AA, with a phase 2 trial initiated in August 2022 in China for severe AA. We expect to complete patient enrollment of this trial in the second half of 2023.

The table below sets forth our clinical development plan for A223:

Indication	Trial phase	Trial status	(Expected) Trial start date	Expected trial end date	Location
Moderate-to-severe RA	Phase 3	CDE clinical consultation	(2H 2023)	2H 2025	China
Severe AA	Phase 2	Ongoing	August 2022	2H 2024	China

Summary of Clinical Trial Data

We initiated a phase 1 clinical trial in healthy subjects in China in October 2018 and completed this trial in March 2020. We also initiated two phase 1b trials in RA patients in China in October 2019 and June 2021, and completed these two trials in June 2022 and July 2022, respectively. We initiated an ongoing phase 2 trial in December 2020 to evaluate the safety and efficacy of A223 in patients with moderate-to-severe RA. For severe AA, we received IND approval in March 2022 and initiated a phase 2 clinical trial in China in August 2022. Set forth below is a summary of the key data from A223's completed and ongoing clinical trials.

Phase 2 Clinical Trial for Moderate-to-severe RA

This is a multi-center, double-blind, randomized, placebo-controlled trial to evaluate the safety and efficacy of A223 versus MTX in patients with moderate-to-severe RA. This trial plans to enroll 160 subjects across 31 clinical research centers in China.

Trial Objectives. The primary endpoint is the American College of Rheumatology (ACR)20 response rate, which is a well-established standard that measures twenty percent improvement in patients' RA symptoms. The secondary endpoints are the proportion of patients who achieved ACR50/70, the proportion of patients who achieved remission or low disease activity, change of patients' health status.

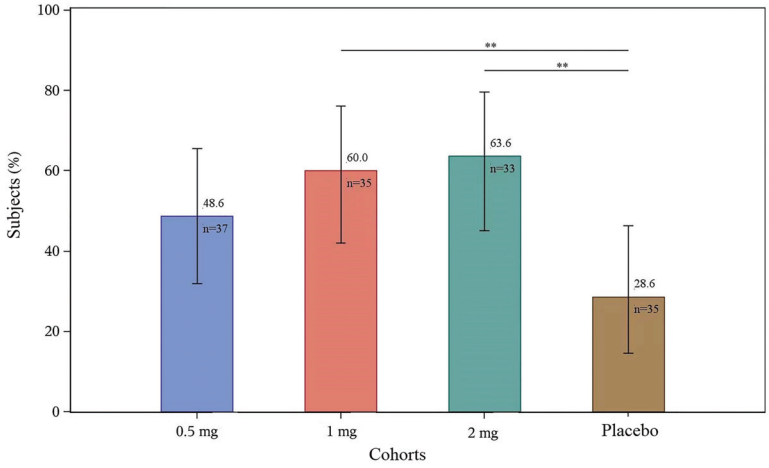
Trial Progress. As of the Latest Practicable Date, this trial was ongoing with patient enrollment completed in November 2022. 160 patients were randomized into 0.5 mg (N=40), 1 mg (N=40), 2 mg (N=39) dose cohorts to receive the corresponding dose of A223 once daily and MTX once weekly, or the placebo cohort (N=41) to receive MTX tablet once weekly.

Trial Design. The trial consists of two parts. In part A, subjects were randomized 1:1:1:1 to receive MTX tablet once weekly plus 0, 0.5, 1, or 2 mg of A223 oral capsule once daily for 12 consecutive weeks. In part B, which begun after the completion of part A, subjects who received 0 mg of A223 oral capsule are randomized 1:1 into A223 0.5 mg and 1 mg cohorts, and those who received 0.5, 1, and 2 mg of A223 continue to receive the same dose once daily for 12 consecutive weeks.

Based on preliminary data as of the data cut-off date (December 27, 2022), A223 demonstrated a dose-dependent ACR20 response (primary endpoint) in moderate-to-severe RA patients, with an ACR20 response of 48.6%, 60.0% and 63.6% in the 0.5 mg, 1 mg and 2 mg A223 dose cohorts. In particular, the ACR20 responses of the 1 mg and 2 mg A223 cohorts were substantially and statistically significantly higher than that of the placebo cohort (28.6%), as illustrated in the diagram and bar chart below.

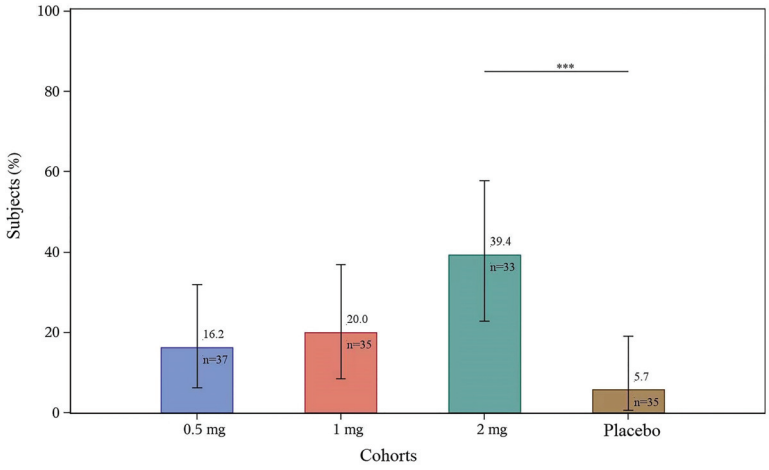
	A223 0.5 mg	**A223 1 mg**	**A223 2 mg**	**Placebo**
Patient number	37	35	33	35
ACR20 (%)	48.6	60.0	63.6	28.6
ACR20 difference between treatment cohort and placebo cohort (%)	20.1	31.4	35.1	
P-value	0.081	0.008	0.004	

ACR20 responses of A223 vs. placebo in moderate-to-severe RA patients



Further, A223 demonstrated a dose-dependent ACR50 response (secondary endpoint), with a substantially and significantly higher (p-value < 0.05) ACR50 difference between the 2 mg A223 cohort and the placebo cohort, as shown in the bar chart below. Moreover, compared with the placebo cohort, other secondary endpoints, including DAS28-ESR<2.6, DAS28-CRP≤3.2, DAS28-ESR≤3.2 and HAQ-DI score, in the 2mg A223 cohort at week 12 were significantly improved (p-value < 0.05).

ACR50 responses of A223 vs. placebo in moderate-to-severe RA patients



Safety Data. Based on preliminary data as of the data cut-off date (December 27, 2022), A223 was generally safe and well-tolerated. The overall incidence of TEAEs across the A223 treatment cohorts (52.5%) was comparable to that of the placebo cohort (58.5%) and there was no obvious dose-dependent incidence of TEAEs in the treatment cohorts. One patient (2.5%) with grade three or above TEAE occurred in each of the 0.5 mg and 1 mg A223 cohorts, and two patients (4.9%) with grade three or above TEAE occurred in the placebo group. All other TEAEs were mild or moderate (grade $\leq$ 2), with the majority of them being grade 1. The following table summarizes the incidence of TEAEs as of the data cut-off date.

	A223 0.5mg (N=40) n *(%)*	**A223 1mg (N=40) n** *(%)*	**A223 2mg (N=38) n** *(%)*	**A223 treatment cohorts total (N=118) n** *(%)*	**Placebo cohort (N=41) n** *(%)*
Any TEAE	19 (47.5)	24 (60.0)	19 (50.0)	62 (52.5)	24 (58.5)
Study drug-related TEAE[1]	10 (25.0)	13 (32.5)	13 (34.2)	36 (30.5)	10 (24.4)
≥ Grade 3 TEAE	1 (2.5)	1 (2.5)	0	2 (1.7)	2 (4.9)
TEAE that led to death	0	0	0	0	0

Note:

(1) As of the data cut-off date (December 27, 2022), there were 159 patients who received at least one dose of A223 or placebo and were evaluable for safety assessment.

Conclusion. Based on preliminary data, A223 demonstrated promising anti-rheumatic efficacy, indicated by substantially and statistically significantly higher ACR20 responses at 1 and 2 mg as well as ACR50 response at 2 mg compared to placebo. A223 also exhibited a good safety profile with most TEAEs being mild or moderate.

Phase 2 Clinical Trial for Severe AA

This is a multi-center, double-blind, randomized, placebo-controlled trial to evaluate the safety and efficacy of A223 in patients with severe AA. The trial plans to enroll 176 adults (≥18 years and ≤65 years), who have 50% or greater scalp-hair loss, in 29 clinical research centers in China.

Trial Objectives. The primary endpoint is the proportion of patients with the Severity of Alopecia Tool (SALT, a method to assess the extent of scalp-hair loss in AA patients) score ≤20 by week 24. The secondary endpoints include the proportion of patients with SALT score ≤20 by week 36, SALT score ≤10 by week 24 and 36, 50% and 75% improvement of SALT relative to baseline by week 24 and 36, as well as changes of SALT relative to baseline by week 24 and 36 and the exposure-response relationship of A223 in patients with severe AA.

Trial Progress. As of the Latest Practicable Date, patient enrollment of this trial was ongoing, with first-patient-in achieved in November 2022.

Trial Design. Subjects are randomized 1:1:1:1 into either the treatment cohorts to receive 0.5, 1 or 2 mg of A223 oral capsule once daily for 36 consecutive weeks, or the placebo cohort.

Phase 1b Drug-drug Interaction Clinical Trial with MTX for Moderate-to-severe RA

This was a multi-center, double-blind, randomized trial to evaluate the PK and safety profile of A223 in combination with MTX in patients with moderate-to-severe RA. This trial was conducted in 31 subjects across eight clinical research centers in China.

Trial Objectives. The primary endpoints were the PK profiles of A223, MTX, and their metabolites 7-OH. The secondary endpoint was the safety of A223 and MTX.

Trial Progress. This trial was completed in July 2022.

Trial Design. All subjects received a single dose of 10 mg of MTX oral tablet on day 1 and day 8 and a single dose of 2 mg of A223 oral capsule once daily from day 3 to day 14.

Safety Data. The combination treatment of MTX and A223 was generally safe and well-tolerated. There was no incidence of TEAEs that led to temporary treatment withdrawal, treatment discontinuation and death. Most TEAEs were mild or moderate (grade ≤ 2) and reversible without additional medical intervention, with the most common ones being elevated level of blood lipids and abnormal blood cell count. One SAE was reported and it was considered by the trial investigator to be possibly unrelated to the study drug.

PK Data. PK analysis in 31 patients showed that the combination treatment of MTX and A223 did not affect major PK parameters including C_{max}, time to peak drug concentration and AUC.

Conclusion. Combination treatment of A223 with MTX exhibited good drug compatibility based on the safety and PK data, supporting the potential of A223 as part of MTX combination therapy with low risks of serious side effects and undesirable PK behaviors.

Phase 1b Clinical Trial for RA

This was a double-blind, randomized, placebo-controlled trial to evaluate the safety, tolerability, PK/PD of A223 and to explore the safe and effective dose range of A223 in patients with RA to provide the basis for the dosing regimen of A223 in subsequent phase 2 trials. The trial was conducted in 30 subjects in one clinical research center in China.

Trial Objectives. The primary endpoint was the safety of A223. The secondary endpoints were the PK/PD profile of A223, ACR20/50/70 response rates, the proportion of patients who achieved remission or LDA and health status of RA patients.

Trial Progress. This trial was completed in June 2022.

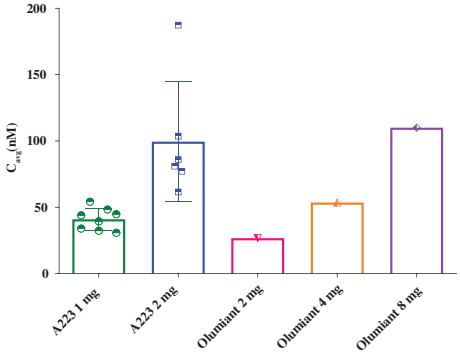
Trial Design. Subjects were randomized to receive a single dose of either 1, 2, or 4 mg of A223 oral capsule or placebo. After completing a single dose and a subsequent 7-day washout period, subjects continued to receive the same dose once daily for 14 days.

Efficacy Data. A223 demonstrated potential efficacy in patients with moderate-to-severe RA after two weeks of treatment. A223 treatment at 2 mg showed the highest efficacy as measured by ACR20 response rate (37.5%), while ACR20 response rate in the placebo cohort was 16.7%.

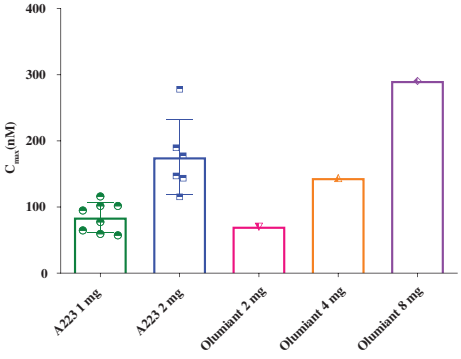
Safety Data. A223 were generally safe and well-tolerated. All AEs were mild or moderate (grade $\leq$2) and were reversible without additional medical intervention. The most common AEs were abnormal blood lipids and abnormal blood cell count.

PK Data. PK in RA patients showed similar trends to those in healthy individuals. As shown in the diagrams below, in non-head-to-head cross-trial comparison with Olumiant, A223 demonstrated significantly lower levels of C_{max} than Olumiant at comparable levels of C_{avg}. This suggested that A223 may have a lower minimum effective dose than Olumiant and thus may be potentially safer and better tolerated while maintaining comparable efficacy as Olumiant.

C_{avg} exposure in RA patients after reaching the steadystate with multiple doses of A223 and Olumiant



C_{max} exposure in RA patients after reaching the steadystate with multiple doses of A223 and Olumiant



Sources: *Olumiant: Olumiant's FDA filing documents*

Conclusion. A223 demonstrated potential efficacy in moderate-to-severe patients with a good safety profile and PK properties consistent with those observed in healthy individuals. Based on PK analysis results, A223 may have a lower minimum effective dose than Olumiant, suggesting that it may be potentially safer and better tolerated while maintaining comparable efficacy as Olumiant.

Phase 1 Clinical Trial in Healthy Subjects

This was a double-blind, randomized, placebo-controlled trial to evaluate the safety, tolerability, PK/PD activity, dosing schedule and the effect of A223 on QTcF interval, an electrocardiogram measurement of cardiac electrical properties, in healthy Chinese subjects. The trial was conducted in 79 subjects in one clinical research center in China.

Trial Objectives. The primary endpoint was the safety of A223. The secondary endpoints were the PK/PD profile and QTcF interval parameters of A223.

Trial Progress. This trial was completed in August 2019.

Trial Design. The trial consisted of single-dose and multi-dose phases. In the single-dose phase, subjects were randomized to receive 1, 2, 4, 6, 8, 10, 15, or 20 mg of A223 oral capsule or placebo. Subjects who completed a single dose of 2, 4 and 6 mg of A223 oral capsule underwent a 120-hour washout period with safety/tolerability assessment. Subjects who completed the washout period with no reported safety issues would be selected for the multi-dose phase. The subject's dose level in the multi-dose phase was the randomized dose (2, 4, or 6 mg) administered in the single dose phase, with subjects receiving A223 capsule once daily for seven consecutive days.

Safety Data. A223 was generally safe and well-tolerated. There was no reported incidence of SAEs, AEs of grade 3 or above, or AEs that led to premature treatment withdrawal. All reported TEAEs were mild or moderate (grade $\leq$ 2), with the majority of them hematologically related, including decreased percentages/counts of neutrophils, lymphocytes, white blood cells and red blood cells in the blood. All reported TEAEs were rapidly reversible within two to three days after A223 treatment without additional medical intervention. The following table summarizes the incidence of TEAEs.

Event	**A223 dose cohorts (N=62) Total (n, %)**	**Placebo cohort (N=16) Total (n, %)**
Any TEAE	55 (88.7)	13 (81.3)
Drug-related TEAE[(1)]	54 (87.1)	13 (81.3)
TEAE grade 1[(2)]	38 (61.3)	11 (68.8)
TEAE grade 2[(2)]	17 (27.4)	2 (12.5)
TEAE grade 3 or above[(2)]	0	0

Notes:

(1) Drug-related TEAEs refer to events classified as related, probably related, or possibly related to the study medication.

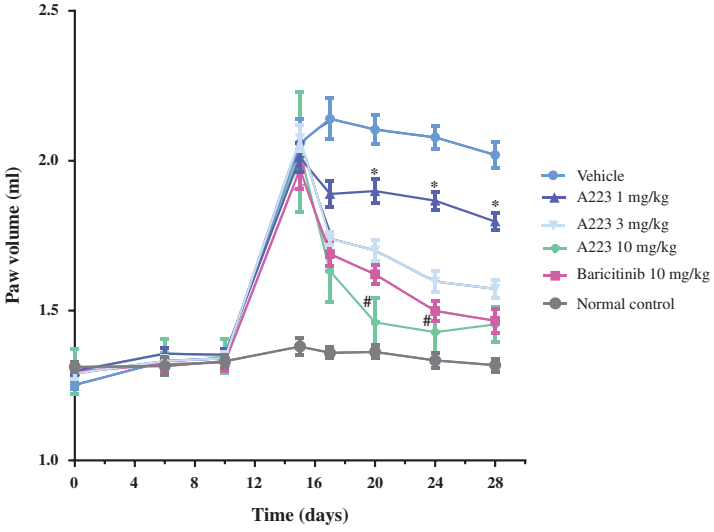
(2) TEAE severity was calculated and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (standard version 5.0).

PK Data. After single-dose administration, A223 demonstrated a half-life between 14.02 to 17.76 hours (h), average oral clearance between 2.75 to to 3.50 L/h and average apparent volume of distribution during terminal phase (V_z/F) between 61.53 to 78.30 L. After multiple-dose administration, A223 demonstrated a half-life between 15.79 to 17.89 h, average CL/F between 2.45 to 3.11 L/h and average V_z/F between 60.79 to 76.31 L.

Conclusion. A223 exhibited a good safety profile in healthy participants with desirable PK properties.

Summary of Preclinical Data

We studied A223 and Olumiant (baricitinib) head-to-head in a (CIA) rat model, which is a widely used *in vivo* model to mimic joint inflammatory symptoms in RA. As shown in the diagram below, the onset of arthritis appeared on about Day 10 with peak onset on about Day 14, as indicated by significantly more paw swelling (expressed as an increase in paw volume) compared to normal control. Daily treatment of A223 at 1, 3 and 10 mg/kg and baricitinib at 10 mg/kg substantially reduced paw swelling, indicated by the reduced paw volume following drug administration on Day 15 compared to vehicle. Notably, CIA rat treated with A223 at 3 mg/kg showed paw swelling reduction comparable to that of baricitinib at 10 mg/kg, while those treated with A223 at 10 mg/kg had a greater paw swelling reduction than baricitinib at the same dose, indicating that A223 may have a lower effective dose than baricitinib.



Notes:

*: A223 1 mg/kg compared with vehicle, p-value < 0.01

#: A223 10 mg/kg compared with baricitinib, p-value < 0.05

Next Steps

Based on the preliminary results from A223's phase 2 trial in moderate-to-severe RA patients, we are consulting the CDE regarding the design of a pivotal phase 3 trial. We expect to initiate the pivotal phase 3 trial in the second half of 2023. For severe AA, we expect to complete patient enrollment of our ongoing phase 2 trial in the second half of 2023.

A223 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

A277 – A Peripherally-restricted KOR Agonist

A277 is potentially one of the first peripherally-restricted KOR agonists for treating CKD-aP in China, a distressing chronic itching condition with large and underserved patient population. As of the Latest Practicable Date, there were no approved treatments specifically targeting CKD-aP in China. KOR agonists have been shown to inhibit pruritus, by counteracting the pro-itching effects of mu opioid receptors (MORs), in both animals and humans. Selectively activating peripheral KORs thus represents a promising therapeutic approach for treating CKD-aP, supported by the recent FDA approval of Korsuva as the first and only peripherally-restricted KOR agonist to date for treating moderate-to-severe CKD-aP.

CKD-aP is a common condition of intense and systemic itchy skin for patients with CKD. It is more prevalent in patients on hemodialysis and those with advanced CKD, affecting over 60% of hemodialysis patients and 40% of ESRD patients. According to Frost & Sullivan, the prevalence of CKD increased from 120.4 million in 2017 to 140.8 million in 2022 and is projected to reach 171.9 million in 2030. According to the same source, there were five peripherally-restricted KOR agonists candidates in phase 1 or beyond in China for CKD-aP as of the Latest Practicable Date.

A277 is a novel peripherally-restricted KOR agonist that selectively activates KORs, but not mu opioid receptors (MORs) or other opioid receptors. A277 is specifically designed to restrict its entry into the CNS and limit its action selectively to KORs on sensory nerves outside the brain and on certain immune cells, thereby potentially minimizing opioid-induced drug dependence, respiratory depression and constipation, as well as dysphoria and hallucination associated with centrally-acting KOR agonists. A277 demonstrated potential efficacy and good safety in a completed phase 1b clinical trial, where it exhibited potential in reducing the pruritus numerical rating scale, a widely adopted standard for evaluating itch intensity, in maintenance hemodialysis patients with moderate-to-severe CKD-aP, with no incidence of opioid-induced drug dependence, respiratory depression and constipation. These positive clinical results indicate the potential of A277 as a safe and effective therapeutic option for CKD-aP.

We are actively progressing the clinical development of A277 in China. We initiated a phase 1 clinical trial in healthy subjects in China in November 2018 and completed this trial in January 2021. We also initiated a phase 1b trial in maintenance hemodialysis patients with moderate-to-severe pruritus in China in August 2020. Having completed this phase 1b trial in January 2022, we commenced a phase 2 trial in maintenance hemodialysis patients with moderate-to-severe pruritus in China in September 2022. We expect to complete this trial in the first half of 2024.

A277 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

SKB378 – A TSLP mAb

SKB378 is potentially the first domestically developed TSLP mAb in China for treating patients with moderate-to-severe asthma, a prevalent chronic airway disease and a primary cause of morbidity and socioeconomic burden worldwide. The current mainstay treatment options of moderate-to-severe asthma are only effective for patients with a specific asthma inflammatory phenotype, underscoring a significant unmet need for innovative therapies applicable to a broader population of asthma patients.

SKB378 targets TSLP, an important cytokine implicated in the pathophysiology of asthma as a key orchestrator of the underlying inflammation. Asthma can be broadly classified into two clinical inflammatory phenotypes, eosinophilic and noneosinophilic, which are respectively characterized by type 2 and non-type 2 inflammation with distinct immune response patterns. Given the major role of TSLP in both types of asthma based on recent published studies, targeting TSLP represents a promising strategy for treating asthma without phenotypic limitations. According to Frost & Sullivan, the prevalence of moderate-to-severe asthma in China rose from 21.5 million in 2017 to 23.6 million in 2022. This number is expected to reach 27.4 million in 2030.

Currently, the approved treatment options of moderate-to-severe asthma in China are mAbs that target type 2 inflammatory pathways and are thus ineffective for patients with noneosinophilic asthma, which account for approximately 50% of moderate-to-severe asthma cases. Tezepelumab, a TSLP mAb that achieved effective asthma control and exacerbation reduction regardless of patients' (non)eosinophilic phenotypes, is the only anti-TSLP treatment approved in the U.S. for severe asthma. As of the Latest Practicable Date, there were nine anti-TSLP therapies in phase 1 or beyond in China.

We received IND approval from the NMPA in February 2022 and initiated a phase 1 clinical trial in healthy subjects in August 2022 in China, which we expect to complete in the second half of 2023.

SKB378 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

SKB336 – A FXI/FXIa mAb

SKB336 is a novel FXI/FXIa mAb designed as an anticoagulant for preventing and treating thromboembolic disorders, starting with venous thromboembolism (VTE) after total knee arthroplasty (TKA). Thromboembolic disorders are prevalent and potentially fatal conditions in which abnormally formed blood clots block blood vessels. The current mainstay anticoagulant therapies put patients at increased risks of severe and potentially life-threatening bleeding complications as their targets are also required for normal coagulation, leaving a substantial unmet need for novel effective anticoagulation agents with limited risk of bleeding.

FXI/FXIa have emerged as a promising anticoagulation target as these factors are not essential for initiating normal blood coagulation, but play a central role in promoting thrombosis, which refers to abnormal coagulation that leads to blood clots developing in a blood vessel. In published preclinical studies, FXI/FXIa deficiencies led to clot instability and prevented the occlusion of blood vessels, suggesting that targeting FXI/FXIa is potentially a safe and effective strategy for preventing and treating thromboembolic disorders, such as VTE after TKA.

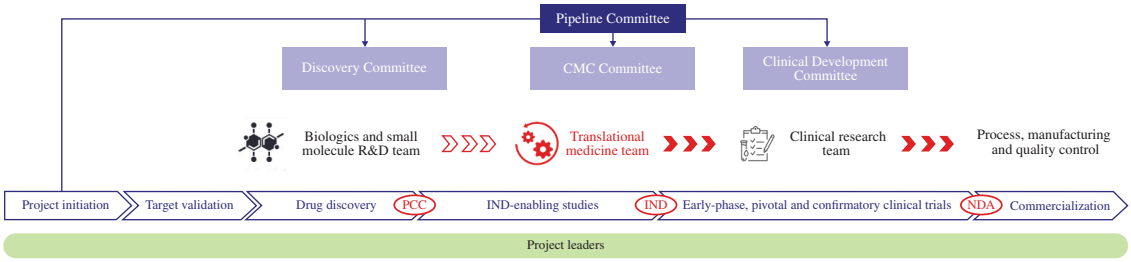
According to Frost & Sullivan, VTE is the third leading vascular diagnosis after heart attack and stroke in China, affecting approximately 3.2 million people in 2022. VTE is commonly triggered by cancer, immobilization, hospitalization and surgery, such as TKA, a common procedure for treating end-stage osteoarthritis. According to the same source, the number of TKA in China grew from 240.1 thousand in 2017 to 360.8 thousand in 2022 at a CAGR of 8.5%, and is projected to rise to 2.9 million in 2030 at a CAGR of 29.8%. As of the Latest Practicable Date, there were no anti-FXI/FXIa drugs approved by the NMPA and two anti-FXI/FXIa drugs were in phase 1 or beyond in China. According to Frost & Sullivan, SKB336 is the first domestically developed anti-FXI/FXIa drug to enter clinical stage in China.

We received IND approval from the NMPA in July 2021 for preventing and treating thromboembolic disorders. We initiated a phase 1a clinical trial in healthy subjects in July 2021 and completed this trial in November 2022.

SKB336 MAY NOT ULTIMATELY BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED.

INTEGRATED DRUG DEVELOPMENT CAPABILITIES

We have developed integrated capabilities encompassing all key drug development functionalities, including R&D, manufacturing, quality control and commercialization, illustrated by the diagram below.



Our drug development capabilities are governed by a well-established management system that covers all key business functionalities, which provides a framework for our internal teams to engage in constructive dialogue and evaluation, particularly when making critical decisions for each drug development plan. Meanwhile, we implement a dynamic global business development strategy to maximize the commercial value of our pipeline in major international markets, leveraging our experience in forging strategic partnerships worldwide.

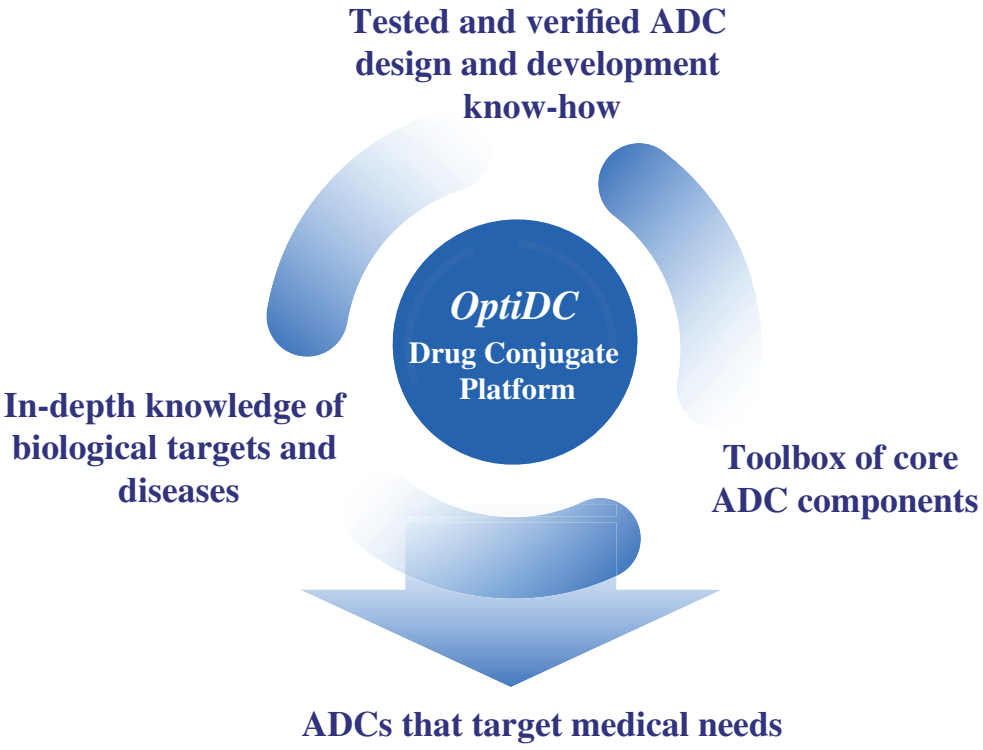
We operate a three-tiered decision-making model, consisting of: (i) a pipeline committee led by our CEO that oversees the entire lifecycle of drug development programs, (ii) discovery, CMC, and clinical development committees that serve as gatekeepers for the progress and quality of our drug development programs, and provide timely feedback in each round of planning, and (iii) project leaders that are instrumental to the effective coordination among different functional groups to ensure smooth execution of our drug development plans.

OUR TECHNOLOGY PLATFORMS

We have established three core platforms with proprietary know-how in ADC, biologics and small molecule technologies that serve as the foundation of our discovery and development of innovative medicines for medical needs in selected disease areas, such as oncology, autoimmune diseases and metabolic diseases. These platforms cover the entire R&D process for different drug modalities and are integrated to allow cross-functional synergies at crucial stages of drug development.

ADC Platform

Our ADC platform, *OptiDC*, is supported by three capability pillars – in-depth knowledge of biological targets and diseases, tested and verified ADC design and development know-how, and a toolbox of core ADC components. Through over a decade of development, we have developed a toolbox of core ADC components which gives us the versatility to engineer customized ADCs optimized for different biological targets to address medical needs in a broad range of indications. We have honed our expertise in ADC process development, manufacturing and quality control, which we believe is crucial in bringing our ADCs from bench to bedside. Notably, our ADC platform is tested and verified through preclinical studies and clinical trials with over 1,160 patients as of the Latest Practicable Date.



Our ADC design strategies are exemplified by *Kthiol*, our proprietary drug-linker strategy implemented in SKB264 that features an optimized balance between safety and efficacy. *Kthiol* incorporates moderately potent payload and irreversible linker conjugation to the antibody, which reduces off-target toxicity as well as on-target off-tumor toxicity of SKB264. Meanwhile, pH sensitive cleavable moiety in the linker allows efficient release of payload once reaching the tumor to improve efficacy. For more details, see "– Our Pipeline – Oncology Franchise – ADCs – SKB264 – Drug Design and Mechanism of Action."

Key capabilities and technologies of our ADC platform encompass all major aspects of ADC development, including the following:

Antibody discovery and optimization. We have developed a bioinformatics-aided antibody discovery workflow with a repertoire of high-throughput screening systems and a robust antibody optimization workflow that involves careful assessment of antibody candidates based on critical developability, efficacy and safety parameters. These workflows allow us to produce antibodies with better target selectivity and broader therapeutic window, as well as enabling us to select optimized combination strategies of antibody with payload-linker for our ADC candidates. For details, see "– Our Technology Platforms – Biologics Platform."

Payload screening. We have constructed an extensive library of cytotoxic small molecules and developed a smooth workflow to screen hundreds of linker-payload combinations *in vitro*/*in vivo* simultaneously. This enables us to efficiently identify payload molecules with desirable cytotoxicity, bystander killing capability, plasma stability, half-life and mechanisms of action that may overcome drug resistance. Leveraging our small molecule

platform, we have in-house developed a range of proprietary payload small molecules with various modes of action (e.g. cytotoxic killing and immune modulation) for pairing with different types of linkers, providing us with the versatility to achieve optimized payload-linker combinations tailored to target indications and molecular targets.

Linker modification. An ideal linker should (i) anchor the payload to the antibody stably in the circulation and release it selectively and efficiently in the tumor; and (ii) possess chemical moieties that increase overall hydrophobicity of ADC to avoid aggregation and fast clearance in the body before bringing efficacy. Leveraging our expertise on linker chemistry, we are able to create reasonably stable and hydrophilic linkers with selective cleavage in the tumor to reduce undesirable toxicities and improve therapeutic window.

Proprietary conjugation technologies. The way a linker-payload conjugates to an antibody influences the DAR as well as the stability and undesirable toxicities of the final ADC product. We have developed proprietary conjugation technologies that enable us to customize the DAR of our ADCs, which is instrumental for creating different combinations of payload toxicity and the amount of conjugated payload molecules to balance the anti-tumor potency and safety profile of each ADC.

In particular, our proprietary linker and conjugation technologies enable us to achieve site-specific and quantity-specific conjugation, without the need to modify the antibody, which is a commonly used industry practice for ADC conjugation. This allows us to produce ADCs with (1) stable conjugation and a lower risk of premature release of payload-linker in circulation, compared to other linker technology used by certain other ADC companies; (2) high homogeneity with a uniform pre-specified DAR, which leads to more consistent PK profiles and hence ADC activity, compared to ADCs that use conventional non-site-specific conjugation; (3) greater ease of engineering and lower cost, compared with ADCs engineered through antibody modifications.

Our ADC technology platform is seamlessly integrated with our manufacturing capabilities, enabling in-house production of antibodies (mAb and bsAb), linkers, payload/small molecules and final ADC products at lab, pilot and commercial scales. This allows us to continuously accumulate deep understanding of, and refine know-how on, the end-to-end development of various types of ADCs, which is integral to our ability to develop innovative ADCs with differentiated features and competitive edge.

We are establishing novel ADC designs to further advance our ADC portfolio via a multi-pronged strategy, including:

- further optimizing our payload/linker technologies to solidify our ADC capabilities, such as (i) our proprietary thiobridge linker, a next-generation linker design that enables site-specific and fixed-DAR conjugation of linker-payload, and (ii) linker with optimized hydrophilicity and stability to improve ADC PK properties and safety window;

- developing bsADCs equipped with dual-targeting antibodies to deliver enhanced clinical benefits, such as (i) biparatopic antibodies that target different, non-overlapping binding sites on a single antigen to improve efficacy by promoting cellular uptake of an ADC, (ii) bsAbs that target two different antigens co-expressed on the same cancer cells to improve binding specificity toward cancer cells and reduce off-tumor toxicity, and (iii) TAA-IO bsAbs to enhance anti-tumor effect by simultaneously targeting TAA on tumor cells (to induce tumor cell death by activating cell death programs or inhibit pro-survival or proliferative signalling) and IO antigen (to eliminate checkpoint inhibition, engage immune effector cells, or promote release of cytokines that facilitate immune crosstalk and anti-tumor immunity);

- developing other novel ADC designs such as iADCs, RDCs, dual-payload ADCs. For example, we are harnessing the synergy between IO and tumor targeting via iADCs, which are a novel form of ADCs to activate anti-tumor immune response on top of conventional tumor-directed cytotoxin delivery, with promising efficacy and safety results observed in preclinical studies. Moreover, we are developing RDCs that carry radioactive isotopes to cancer cells. By manipulating a distinct mechanism of action, RDCs represent a promising strategy to overcome drug resistance associated with traditional cytotoxin-based ADCs. We are also developing linkers that allow dual-payload delivery to harness multiple mechanisms of action to enhance treatment responses; and

- developing ADCs with non-cytotoxic payloads to target non-oncology diseases. In addition to ADCs for treating cancers, we are developing ADCs configured with various novel, non-cytotoxic payload strategies for non-oncology diseases, such as ADCs with GR modulators as payloads to treat autoimmune diseases.

As a forerunner in ADC research and development, we are a lead participant in formulating China's first set of technical guidelines and industry standards on ADC drug development, such as the "Technical Guidelines for Clinical Development of Anti-tumor ADC Drugs (Consultation Paper)" (《抗腫瘤抗體偶聯藥物臨床研發技術指導原則(徵求意見稿)》) published by the CDE in September 2022 and the "Expert Consensus on ADC Drug Quality Control and Preclinical Assessment" (《抗體偶聯藥物質量控制和臨床前評價專家共識》) released in July 2018.

Biologics Platform

We have developed an extensive biologics technology platform capable of delivering quality and innovative mAbs and bsAbs to advance our pipeline of ADCs, immunotherapies and targeted therapies. The competitive edge of our biologics platform is underscored by its end-to-end antibody development capabilities ranging from antibody discovery and optimization, to bioprocessing, scale-up manufacturing and quality control, which has allowed us to successfully and efficiently advance multiple ADC, mAb and bsAb candidates to clinical stage. The core capabilities of our biologics platform are illustrated below:

Antibody discovery. We have built a bioinformatics-aided antibody discovery workflow to systematically modify the protein sequence of antibodies and identify those with desirable pharmacological properties and biological activities using a repertoire of high-throughput screening systems including hybridoma, phage display, single B cells and de novo sequencing.

Our antibody discovery workflow is highlighted by: (i) a highly efficient antibody discovery platform featuring optimized animal immunization and hybridoma fusion technologies, a fully human phage library with large capacity and diversity, as well as single B cell technologies and de novo antibody sequencing technologies; (ii) antibody evaluation platform equipped with high-throughput natural conformation target and endocytosis screening methods, systematic and scientific evaluation of drug efficacy *in vivo* and *in vitro* for cancer, autoimmunity, metabolism and other diseases, as well as developability assessment for early stage antibody discovery, including post-translational modifications, hydrophobicity, stability and immunogenicity; (iii) antibody engineering platform that features antibody humanization and physicochemical property modification, affinity maturation, antibody-target docking based on artificial intelligence technology, and specific bsAb design and construction; (iv) high yield antibody expression platform using in-house developed cell biology technologies, such as different vector construction and transfection methods that enable high transfection rate. Our antibody discovery workflow is optimized for the discovery of therapeutic antibodies, allowing seamless transition into development and manufacturing.

Antibody optimization. Building on our antibody discovery workflow, we have established a robust antibody optimization workflow that enables us to produce antibodies with better target selectivity and wider therapeutic window. This workflow comprises five major stages (from target research and antibody generation, to lead selection, lead optimization and preclinical enabling) and involves careful assessment of critical developability, efficacy and safety parameters. This allows us to generate antibody candidates with promising developability, efficacy and safety profiles.

Bioprocessing and scale-up manufacturing. We have a comprehensive in-house system that covers all the upstream and downstream bioprocessing steps throughout the development lifecycle of biologics candidates. It features (i) a cell culture platform with standardized process development and scale-up capacity, with flexible cell culture modes and capability of developing chemical-defined medium formulation, (ii) a well-established ADC conjugation and purification platform, and (iii) a formulation platform capable of developing various dosage forms such as high-concentration, lyophilized and pre-filled formulation, all of which contribute to the manufacturing of high-quality biologics candidates for clinical trial use.

Small Molecule Platform

We have built an innovative small molecule platform focusing on target validation, molecule innovation and translational R&D. The competitive edge of our small molecule platform lies in the integration of medicinal chemistry and CADD technologies, which enable us to efficiently and scientifically identify optimized PCC molecules. Our integrated medicinal chemistry and CADD technologies are highlighted by molecular docking, pharmacophore modeling, virtual screening and ADMET prediction. Through computer simulation and calculation, CADD allows a more scientific and reasonable analysis of potential drug-target interactions. It also facilitates the prediction of key drug-like properties of potential drug candidates and the use of virtual screening to rapidly screen potential compounds from databases with over tens of thousands of chemical compounds.

These capabilities enable a more efficient and productive preclinical drug discovery by allowing us to focus on compound optimization in early-stage research, thus reducing the number of compounds synthesized for each project and significantly shortening the time required for delivering preclinical candidate. Since its inception in 2014, our small molecule platform has been instrumental in advancing innovative small molecule drug candidates for treating various cancers and chronic diseases, including four clinical-stage assets. We are also exploring state-of-the-art technologies such as PROTAC to navigate challenging protein targets.

RESEARCH AND DEVELOPMENT

We believe research and development is critical to our future growth and our ability to remain competitive in the global biopharmaceutical market. Our integrated in-house R&D capabilities, built on our three technology platforms, give us control and visibility over our R&D process, reduces our reliance on CROs, and enable us to ensure the quality and efficiency of our drug development programs. For details regarding our technology platforms, please see "– Our Technology Platforms."

We conduct our research and development activities primarily through an in-house R&D team, and engage CROs from time to time to support our preclinical research and clinical trials. For the years ended December 31, 2021 and 2022, our costs and expenses in relation to R&D activities, which represented our cost of sales and research and development expenses, were RMB748.2 million and RMB1,122.8 million, respectively. In particular, the costs and expenses in relation to R&D activities for our Core Products amounted to RMB205.9 million (including RMB60.5 million for SKB264 and RMB145.4 million for A166) and RMB461.6 million (including RMB323.6 million for SKB264 and RMB138.0 million for A166) for the years ended December 31, 2021 and 2022, respectively, accounting for 27.5% and 41.1% of our total costs and expenses in relation to R&D activities for the same years, respectively. Such costs and expenses mainly included clinical trial expenses, staff costs and costs of raw materials and consumables during the Track Record Period. We expect that our costs and expenses in relation to R&D activities will increase in line with the future growth of our business.

In-house R&D

Our R&D team comprises industry veterans with extensive experience of driving drug development programs at leading biopharmaceutical companies. As of December 31, 2022, our R&D team had over 760 members, over half of whom held a master's or higher degree (including 63 with a doctoral degree), mainly in medical science, pharmacology, biology and chemistry. When we recruit R&D team members, we primarily take into account the candidates' academic qualifications, relevant industry experience, and whether their expertise complements and synergizes with our accumulated know-how. In particular, when selecting core R&D team members responsible for the development of ADC drug candidates, we further consider the candidates' prior experience in ADC development, whether at academic institutions or with other biopharmaceutical companies, as well as their demonstrated contribution to the advancement of this new drug modality. We believe our established profile in ADC development has enabled us to recruit strong R&D talent in this emerging field.

We operate a highly systematic R&D structure under our three-tiered decision-making model. Our R&D strategy and direction is guided by our pipeline committee, which is led by our CEO and Executive Director, Dr. Ge Junyou. Our R&D team executes the vision and programs set by our pipeline committee, and plays a central role in the development of the Core Products and other pipeline candidates. Our R&D team is further divided into several centers based on the different types of R&D activities performed, including: a clinical research center, a biologics drug center, a small molecule drug center and a translational medicine center. The following table sets forth details of our R&D team as of December 31, 2022:

R&D Centers	Number	% of Total
Clinical research	392	51.2%
Biologics drug	108	14.1%
Small molecule drug	118	15.4%
Translational medicine	82	10.7%
Others	66	8.6%
Total	766	100.0%

Although we believe every role that we have created in our R&D system is important, we consider core R&D team members those who have made meaningful contribution to the discovery and development of the Core Products. These core R&D team members bring with them extensive experience driving drug discovery and development programs at leading MNCs, including Wyeth, LLC (now Pfizer), Pfizer Inc. (NYSE stock code: PFE), Biogen Inc. (NASDAQ stock code: BIIB) and Eli Lilly and Company (NYSE stock code: LLY), as well as leading domestic biopharmaceutical companies. Our core R&D team is led by Dr. TAN Xiangyang (譚向陽), who has over 30 years' experience in the research and development of innovative drugs.

The composition of our core R&D team may change from time to time in line with normal turnover in organizations, the departure of individual members did not, and are not expected to, materially affect our R&D activities or product pipeline. This is because our R&D system is designed to have a large team of capable scientists and researchers and well-coordinated within a balanced structure to reduce reliance on individual members.

None of our R&D team members currently holds any position in the Remaining Kelun Group. Historically, certain of our R&D team members were initially staffed within the Remaining Kelun Group, as our Company was not established until 2016 as a platform dedicated to innovative drug development within Kelun Group. Since inception, we have grown our platform by recruiting R&D personnel, especially those with experience in ADC development, and at the same time, personnel involved in innovative drug research were transferred from the Remaining Kelun Group to our Group to optimize the business delineation of different members within Kelun Group. No R&D personnel currently employed by the Remaining Kelun Group has any meaningful contribution in the development of our Core Products and other pipeline candidates.

During the Track Record Period and in the ordinary and usual course of business, we engaged certain subsidiaries of the Remaining Kelun Group to provide auxiliary R&D services (the "Auxiliary R&D Procurement Services"), which include process development and optimization, sample purification, crystallization screening, GMP batch release testing and packing material release testing. Our Directors are of the view that such Auxiliary R&D Procurement Services provided by the Remaining Kelun Group are supporting services in nature rather than core R&D activities, the latter of which are conducted within our Company. These services do not affect our ability to operate independently from the Remaining Kelun Group. For details, please see "Relationship with our Controlling Shareholders – Operational Independence" and "Connected Transactions – Partially Exempt Continuing Connected Transactions – Procurement and Provision of Auxiliary R&D Services."

The following are the key steps of our R&D process, from project initiation, target validation, drug discovery, preclinical studies, to clinical development:

- ***Project Initiation***. Before initiating a project, our pipeline committee will conduct a comprehensive analysis based on the latest innovations and medical developments in the relevant therapeutic areas, with an aim to assess the market size, patentability, competitive landscape and potential risks involved in a proposed project.

- ***Target Validation and Drug Discovery***. We carry out initial experiments and collect evidence to support our target selection rationale. After a target is validated, we conduct further testing on a candidate's biochemical and biophysical properties, as well as early CMC activities to assess its safety and efficacy profile. At this stage, candidates are further evaluated based on key factors such as scientific rationale, risk and safety, commercial viability, patentability, and upcoming clinical, regulatory and manufacturing plans, to make sure that the final candidate selected is differentiated in the competitive landscape and warrants further investment. Our

drug discovery capabilities are exemplified by our innovative, proprietary ADC design strategies, such as *Kthiol*, our drug-linker strategy to improve ADC stability and reduce off-target and on-target off-tumor toxicity. These ADC design strategies have enabled us to develop ADCs that effectively treat specific types of cancers, including BC, NSCLC and GI cancers, our major indications of interest.

- ***Preclinical Studies***. During the preclinical stage, we assess the PK performance, toxicity, pharmacological and safety profile of the drug candidate through *in vitro* and animal studies. For ADC candidates, we specifically conduct antibody/antigen binding studies, *in vitro* cytotoxic measurements, *in vivo* anti-tumor efficacy analysis, among other tests, to optimize and select the proper compounds for further efficacy and safety studies. Our discovery committee supervises the entire R&D progress and conducts regular meetings to monitor and discuss the progress of each drug candidate, makes suggestions on whether to advance a certain drug candidate to the clinical stage, while allocating resources to different projects in the discovery portfolio. It also determines the timeline for IND application and other key development milestones. Meanwhile, our translational medicine team conducts extensive research encompassing a wide range of studies from DMPK, toxicology and biomarker development, to quantitative and clinical pharmacology, which is critical to facilitating the bridging of our drug discovery and preclinical studies with clinical needs, and improving the success rates, time-efficiency and cost-effectiveness of our clinical trials.

- ***Clinical Development***. During clinical trials, we communicate closely with the trial sites and principal investigators to ensure the clinical trial is conducted in a timely manner and in accordance with the study protocol and good clinical practice (GCP) guidelines, under the supervision of our clinical development committee. We select reputable clinical trial institutions and hospitals based on their quality, resources, experiences, reputation, and availability of experts and patients. Furthermore, our regulatory affairs team oversees the registration strategy and submission of documents required by the relevant regulatory authorities. We also maintain close communication with these authorities, including the NMPA and the FDA, to ensure we are following the regulatory requirements for IND and NDA/BLA approvals.

Collaboration with Third Parties

We are primarily responsible for the R&D of our pipeline assets. Our in-house R&D is supported by the third parties we engage, including auxiliary or administrative services to us by CROs and the Remaining Kelun Group. In addition, we work with third-party collaborators in accordance with responsibilities set out in relevant license and collaboration agreements to conduct certain R&D activities. For details, see "– Our License and Collaboration Arrangements."

In addition to conducting our core R&D activities in-house, we also engage reputable CROs to manage, conduct, and support our preclinical research and clinical trials. The services they provide under our supervision primarily include performing data management and statistical analyses, conducting site management, patient recruitment and pharmacovigilance services in our clinical trials, and carrying out laboratory tests and other tasks based on our needs. We select CROs based on various factors, such as professional qualifications, research experience in the related fields, service quality and efficiency, industry reputation, and pricing. Depending on the type of services needed, we enter into service agreements with our CROs on a project-by-project basis, which set out detailed work scope, sample size, procedures, deliverables, timeline and payment schedule. We closely supervise our CROs to ensure their performance in a manner that complies with our protocols and applicable laws, which in turn protects the integrity and authenticity of the data from our trials and studies.

Key terms of our agreements that we typically enter into with our CROs are set forth below.

- ***Services***. The CRO provides us with services in the course of our preclinical studies and clinical trials, such as implementing animal studies, providing clinical services, record keeping and report preparation.

- ***Term***. The CRO is required to perform its services within the prescribed time limit set out in each work order, usually on a project basis.

- ***Payments***. We are required to make payments to the CROs in accordance with a payment schedule agreed by the parties.

- ***Intellectual property rights***. We own all intellectual property rights arising from the projects conducted by the CROs within the stipulated work scope.

During the Track Record Period and in the ordinary and usual course of business, we engaged certain subsidiaries of the Remaining Kelun Group to provide auxiliary R&D services (the "Auxiliary R&D Procurement Services"), which include process development and optimization, sample purification, crystallization screening, GMP batch release testing and packing material release testing. Our Directors are of the view that such Auxiliary R&D Procurement Services provided by the Remaining Kelun Group are supporting services in nature rather than core R&D activities, the latter of which are conducted within our Company. These services do not affect our ability to operate independently from the Remaining Kelun Group. For details, please see "Relationship with our Controlling Shareholders – Operational Independence" and "Connected Transactions – Partially Exempt Continuing Connected Transactions – Procurement and Provision of Auxiliary R&D Services."

R&D Facilities

As of the Latest Practicable Date, our R&D activities were primarily conducted in Chengdu, Shanghai, and Beijing in China. Our Chengdu headquarters is home to our technology platforms and research laboratories, which are equipped with state-of-the-art equipment and workspace to support our drug discovery, preclinical and clinical needs. In addition, we have established our Shanghai Clinical Center and Beijing Clinical Center, where we house part of our clinical development team. With the collective efforts of our Chengdu, Beijing and Shanghai team, we are able to efficiently manage our drug development plan, clinical protocol design, regulatory affairs and clinical operations across China.

OUR LICENSE AND COLLABORATION ARRANGEMENTS

We believe that an open and collaborative mindset is crucial to the success of our global strategy. Along each step of our drug development plans – from drug discovery to commercialization – we proactively pursue external collaborations, licensing arrangements and other strategic partnerships to create synergies with our pipeline and technology platforms.

Set forth below is a summary of the major terms from our key license and collaboration agreements.

License and Collaboration Agreement with MSD for SKB264

In September 2021, we entered into an option and collaboration agreement with MSD, which was amended and restated as an exclusive license and collaboration agreement (as may be amended from time to time, the "SKB264 Out-license Agreement") in May 2022, as MSD exercised the exclusive option to obtain, and pursuant to which we granted to MSD an exclusive, royalty-bearing and sublicensable license to develop, use, manufacture and commercialize ("Exploit") our TROP2 ADCs, including SKB264 (also known as "MK2870" in MSD's portfolio) and any other TROP2 ADCs we may develop in the future (the "Licensed Compounds"), and products containing one or more such TROP2 ADCs (the "SKB264 Licensed Products") outside Greater China. As of the Latest Practicable Date, SKB264 was the only TROP2 ADC in our pipeline, and therefore the only TROP2 ADC specifically out-licensed to MSD to date, and we had no specific plans to develop other TROP2 ADCs in addition to SKB264.

MSD, one of our Pre-[**REDACTED**] investors and an Independent Third Party, is a U.S.-based multinational biopharmaceutical company focused on researching, developing and commercializing innovative pharmaceutical products. MSD is a global healthcare company with deep expertise in the development of innovative oncology drugs. As part of its focus on cancer, MSD is committed to exploring the potential of immuno-oncology with one of the largest development programs in the industry across more than 30 tumor types, while continuing to augment its pipeline, including through strategic collaborations, and developing new generations of drug candidates such as ADCs. We became acquainted with MSD through industry conferences before the two parties explored opportunities for collaboration.

We also granted MSD a non-exclusive and sublicensable license to use certain of our patents, know-how and clinical data to develop, use and manufacture the Licensed Compounds and the SKB264 Licensed Products within Greater China, solely for the purpose of Exploiting the Licensed Compounds and the SKB264 Licensed Products outside Greater China. In turn, MSD granted to us an exclusive, sublicensable, royalty-free license to use certain of its patents, know-how and clinical data solely for Exploiting the Licensed Compounds and the SKB264 Licensed Products within Greater China. We retain the right to Exploit the Licensed Compounds and the SKB264 Licensed Products for any and all purposes within Greater China. Based on such retained rights, we will continue to advance our clinical development plan for SKB264 in Greater China. For details, see "– Our Pipeline – Oncology Franchise – ADCs – SKB264 – Clinical Development Plan." Each party shall have the right to use all clinical data and results generated from SKB264's clinical trials to support the development, manufacture and commercialization of the Licensed Compounds or SKB264 Licensed Products outside Greater China (in the case of Merck) and within Greater China (in the case of our Company).

We and MSD have established a Joint Steering Committee (the "**JSC**") to discuss the overall coordination and oversight of the activities under the SKB264 Out-license Agreement. The JSC will endeavor to make decisions by consensus, with each of MSD and us having one vote. If consensus is not reached by the parties' representatives pursuant to such vote, then the matter may be escalated by either party to designated executives of both MSD and us with appropriate decision making authority for resolution. In the event the designated executives are unable to resolve the issue within 30 days, then we shall generally have the final decision-making authority with respect to all matters solely pertaining to Greater China, and MSD shall generally have the final decision-making authority with respect to all matters not solely pertaining to Greater China.

Pursuant to the SKB264 Out-license Agreement, we and MSD have agreed to a study development plan, which may be amended from time to time, to govern the research, development, testing and conduct of certain clinical trials and CMC activities, including evaluating the potential of SKB264 as a monotherapy and in combination with Keytruda for selected solid tumors and advanced NSCLC. We have agreed to continue to be the sponsor of the following global clinical trials, as we had already commenced such trials before the SKB264 Out-license Agreement was signed: (i) continue the ongoing global phase 2 dose expansion study of SKB264 (the "Ongoing SKB Clinical Trial"), which is part of our global phase 1/2 trial of SKB264 as monotherapy for selected advanced solid tumors, and (ii) conduct two basket studies (the "Basket Studies"), namely (A) the global phase 2 basket study of SKB264 in combination with Keytruda for selected solid tumors and (B) the standalone NSCLC basket study of SKB264 as monotherapy or combination therapies. MSD may request that the Ongoing SKB Clinical Trial and Basket Studies be transferred to itself, as they have the right and responsibility to develop and commercialize SKB264 outside Greater China.

In the event MSD elects to exercise such right, the parties shall negotiate and agree to a transition plan setting forth each party's obligations in connection with the transfer the details of the transition plan being coordinated and organized by a joint development committee. The joint development committee, a sub-committee under the JSC, is responsible for determining

the details of the transition plan, and coordinate and oversee the transition. If we continue to conduct such trials, MSD shall make quarterly payments to us based on a study budget stipulated under the agreement, which may be adjusted from time to time, upon our provision of interim data package with progress of these clinical trials. We do not anticipate any negative implications if MSD elects to exercise such rights.

In the event that MSD determines that any regulatory filings (other than those that we have already obtained for the Ongoing SKB Clinical Trial and Basket Studies) outside Greater China are required for any activities hereunder, including INDs, NDAs and other marketing authorizations (as applicable), then as between the parties, MSD shall (i) have the sole right, in its discretion, to obtain such regulatory filings and (ii) be the owner of all such regulatory filings. Upon MSD's request, we shall transfer all regulatory filings for SKB264 that we own or control outside Greater China, including any INDs, NDAs and other marketing authorizations (as applicable), to MSD, provided that, to the extent necessary, we shall retain title to such regulatory filings associated with the Ongoing SKB Clinical Trial and/or a Basket Study until its completion or as of the time MSD elects to assume responsibility for such study. Save as disclosed in this paragraph, we retain the sole right to obtain any regulatory filings and be the owner of all such regulatory filings within Greater China.

In partial consideration of the SKB264 Out-license Agreement, we are eligible to receive four one-time payments totaling up to US$102.0 million, of which US$47.0 million had been paid as of the Latest Practicable Date. In addition, MSD agrees to make quarterly payments in connection with SKB264's ongoing research and development activities, the amounts of which are pre-determined and set forth in the agreement, based on a budget agreed between MSD and us. Such budget reflects the costs expected to be incurred by us in performing the R&D activities we have undertaken in relation to SKB264's global clinical trials. To date, we had received a total of US$81.0 million in quarterly payments. Further, we are entitled to future payments up to an aggregate of (i) US$380.0 million upon the achievement of specified development milestones by MSD, and (ii) US$780.0 million upon the achievement of sales-based milestones by MSD. As of the Latest Practicable Date, no milestone payments had become due under this agreement. MSD also agrees to pay us tiered royalties ranging from mid-single-digit to low-double-digit percentage on future annual net sales of the SKB264 Licensed Products outside Greater China, on a product-by-product and country-by-country basis, subject to certain adjustments, until the expiration of the later of (i) the last-to-expire valid patent claim to the applicable SKB264 Licensed Products in a given country; or (ii) a period of ten years following the first commercial sale of the applicable SKB264 Licensed Products in such country.

As of the Latest Practicable Date, the patents we had licensed to MSD included, but are not limited to, one granted patent in China and three pending patent applications (one in China, one in the U.S., and one under the PCT) which we consider material to SKB264's development and commercialization and comprehensively cover SKB264's structure, formulation, method of preparation and use. For details, see "– Intellectual Property." We remain the owner of these licensed patents, while MSD is licensed to utilize these patents owned by us to Exploit the Licensed Compounds and Licensed Products outside Greater China. Inventions arising from

the performance of the SKB264 Out-license Agreement (and any intellectual property rights therein) shall be owned in accordance with inventorship as determined under U.S. patent laws, regardless of where the activities occurred. Each party has the first right to file applications for patent rights invented and owned by itself, upon appropriate consultation with the other party. As we retained the right to Exploit the Licensed Compounds and SKB264 Licensed Products within Greater China, any invention arising from clinical trials conducted solely by us in Greater China would be owned by us. In addition, MSD has the first right to file patent applications under the name of both parties for patent rights jointly invented and owned by MSD and us, and the first right, but not the obligation, to prosecute and maintain, upon appropriate consultation with us, such joint patent rights worldwide.

Unless terminated earlier in accordance with its terms, the SKB264 Out-license Agreement will remain in effect until expiration of all royalty obligations, upon which all licenses granted to MSD under the agreement shall become fully paid-up, perpetual and irrevocable, and all licenses granted to us by MSD shall become perpetual and irrevocable. MSD has the right to terminate the SKB264 Out-license Agreement at any time, in its sole discretion, by giving us a 60 days' advance written notice, in which case each party shall pay all amounts then due and owing as of the termination date. In general, either party may terminate this agreement (i) if the other party is in breach of its material obligations under the agreement, within 60 days after notice from the other party requesting cure of the breach, or (ii) in the event of the other party's bankruptcy, reorganization, liquidation, receivership and similar proceedings. If MSD is entitled to terminate the agreement as a result of our material breach, it may by written notice elect to continue the agreement, in which case: (i) any payments due to us under the SKB264 Out-license Agreement after the date of such written notice (including milestone payments and royalties) shall be reduced to 60% of the initial amount, and (ii) all other terms and conditions of the SKB264 Out-License Agreement shall continue in full force and effect.

License and Collaboration Agreement with MSD for SKB315

In June 2022, we entered into a collaboration and license agreement with MSD, under which we granted to MSD an exclusive, royalty-bearing, sublicensable license to develop, use, manufacture and commercialize ("Exploit") SKB315, our CLDN18.2 ADC, and products based on SKB315 (the "SKB315 Licensed Products") globally (the "SKB315 Out-license Agreement").

We also granted MSD an exclusive and sublicensable license to use our patents and know-how relating to SKB315 to Exploit our CLDN18.2-directed antibodies for medical diagnosis globally, to the extent useful for Exploiting SKB315 and SKB315 Licensed Products. We retain all rights to (i) perform our obligations under the SKB315 Out-license Agreement, and (ii) utilize our technologies, including know-how, patents, and linker and payload technologies, for antibodies or ADC compounds that are not directed to CLDN18.2.

Pursuant to the SKB315 Out-license Agreement, we shall carry out certain activities in support of the clinical development of SKB315 and SKB315 Licensed Products, under the oversight and direction of a joint steering committee ("JSC") and pursuant to a collaboration plan which may be amended by the JSC from time to time (the "Collaboration Plan").

The JSC will endeavor to make decisions by consensus, with each of MSD and us having one vote. If consensus is not reached by the parties' representatives pursuant to such vote, then the matter may be escalated by either party to designated executives of both MSD and us with appropriate decision making authority for resolution. As of the Latest Practicable Date, the Collaboration Plan included an ongoing phase 1a clinical trial of SKB315 in China. We are entitled to reimbursement from MSD for the reasonable and documented costs we incur in performing such development activities, subject to a collaboration budget which may be reviewed and amended by the JSC from time to time. As of the Latest Practicable Date, we had received reimbursement of US$1.96 million from MSD.

Except as expressly provided in the Collaboration Plan, MSD shall have the right and operational responsibility to develop and commercialize SKB315 globally, subject to other applicable terms set forth in the SKB315 Out-license Agreement. Notwithstanding the foregoing, MSD shall discuss with us in good faith with respect to our co-promotion rights for SKB315 in China. Upon MSD's request, we shall transfer all regulatory filings for SKB315 that we own or control, including any INDs, NDAs and other marketing authorizations (as applicable), to MSD.

In partial consideration of the SKB315 Out-license Agreement, MSD paid us an upfront payment of US$35.0 million in September 2022. We are eligible to receive future milestone payments, conditioned upon the achievement of specified development and regulatory milestones, up to an aggregate amount of US$416.0 million. Further, we are entitled to future milestone payments of up to an aggregate of US$485.0 million, conditioned upon the achievement of specified sales-based milestones. As of the Latest Practicable Date, no milestone payments had become due under this agreement. MSD also agrees to pay us tiered royalties ranging from mid-single-digit to low-double-digit percentage on future annual net sales of the SKB315 Licensed Products, on a product-by-product and country-by-country basis, subject to certain adjustments, until the expiration of the later of (i) the last-to-expire valid patent claim to the applicable SKB315 Licensed Products in a given country; or (ii) for a period of ten years following the first commercial sale of the applicable SKB315 Licensed Products in any such country.

Inventions arising from the performance of the SKB315 Out-license Agreement (and any intellectual property rights therein) shall be owned in accordance with inventorship as determined under U.S. patent laws. MSD has the first right to file patent applications under the name of both parties for the patent rights jointly owned by MSD and us. MSD shall have the first right, but not the obligation, to prosecute and maintain, upon appropriate consultation with us, such joint patent rights worldwide.

Unless terminated earlier in accordance with its terms, the SKB315 Out-license Agreement will remain in effect until expiration of all royalty obligations, upon which all licenses granted to MSD under the agreement shall become fully paid-up, perpetual and irrevocable. MSD has the right to terminate the SKB315 Out-license Agreement at any time, in its sole discretion, by giving us a 60 days' advance written notice, in which case each party shall pay all amounts then due and owing as of the termination date, including but not limited to the development costs we may have incurred consistent with the Collaboration Plan. In general, either party may terminate this agreement (i) if the other party is in breach of its material obligations under the agreement, within 60 days after notice from the other party requesting cure of the breach, or (ii) in the event of the other party's bankruptcy, reorganization, liquidation, receivership and similar proceedings. If MSD is entitled to terminate the agreement as a result of our material breach, it may by written notice elect to continue the agreement, in which case: (i) any payments due to us under the SKB315 Out-license Agreement after the date of such written notice (including milestone payments and royalties) shall be reduced to 60% of the initial amount, and (ii) all other terms and conditions of the SKB315 Out-License Agreement shall continue in full force and effect.

License and Collaboration Agreement with MSD for Up to Seven Preclinical ADC Assets

In December 2022, we entered into an exclusive license and collaboration agreement with MSD to develop up to seven preclinical ADC assets for the treatment of cancer. Under this agreement, we granted to MSD exclusive global licenses to research, develop, manufacture and commercialize multiple preclinical ADC assets ("Licensed ADCs") and exclusive options to obtain additional exclusive licenses to certain other preclinical ADC assets ("Option ADCs"). We retain the right to research, develop, manufacture and commercialize certain Licensed ADCs and Option ADCs for China, Hong Kong and Macau.

MSD paid us a non-refundable upfront payment of US$175.0 million in March 2023. We are eligible to receive future milestone payments, conditioned upon the achievement of specified development, regulatory and sales-based milestones, up to an aggregate amount of US$9.3 billion, if all candidates achieve regulatory approval and we do not retain mainland China, Hong Kong and Macau rights for the Option ADCs, plus tiered royalties on net sales for any commercialized ADC product. As of the Latest Practicable Date, no milestone payments had become due under this agreement.

Inventions arising from the performance of this agreement (and any intellectual property rights therein) shall be owned in accordance with inventorship as determined under U.S. patent laws. MSD has the first right to file patent applications under the name of both parties for the patent rights jointly owned by MSD and us, and the first right, but not the obligation, to prosecute and maintain, upon appropriate consultation with us, such joint patent rights worldwide. Unless terminated earlier in accordance with its terms, this agreement will remain in effect until expiration of the respective royalty obligations, upon which all licenses granted to MSD under the agreement shall become fully paid-up, perpetual and irrevocable. MSD has the right to terminate this agreement in whole or in part with respect to a given collaboration program at any time, in its sole discretion, by giving us a 60 days' advance written notice,

provided that no termination shall become effective until we receive the aforementioned upfront payment. Each party shall pay all amounts then due and owing as of the termination date and MSD shall make payment to us for all applicable costs we incurred up to the termination date and not yet paid for (if any). In general, either party may terminate this agreement (i) if the other party is in breach of its material obligations under the agreement, within 60 days after notice from the other party requesting cure of the breach, or (ii) in the event of the other party's bankruptcy, reorganization, liquidation, receivership and similar proceedings. If MSD is entitled to terminate this agreement as a result of our material breach, it may by written notice elect to continue the agreement, in which case: (i) any payments due to us under this agreement after the date of such written notice shall be reduced to 60% of the initial amount, and (ii) all other terms and conditions of this agreement shall continue in full force and effect.

Cooperative Development Agreement with Levena for A166

In March 2014, Kelun Research Institute entered into a cooperative agreement with Concortis, Inc. ("Concortis") to jointly develop A166, our HER2 ADC (as amended and supplemented, the "A166 Co-development Agreement"). An amendment agreement was signed in December 2020 among our Company, Kelun Research Institute, Levena (Suzhou) Biopharma Co., Ltd. ("Levena"), Contortis, and Sorrento Therapeutics, Inc. (NYSE: SRNE), pursuant to which (i) we accepted and assumed all the rights and obligations of Kelun Research Institute, and (ii) Levena accepted and assumed all the rights and obligations of Concortis under the A166 Co-development Agreement. Both Concortis and Levena are affiliates of Sorrento Therapeutics, Inc., an Independent Third Party and U.S.-based clinical and commercial stage biopharmaceutical company specialized in the development of novel cancer therapies.

Pursuant to the A166 Co-development Agreement, we have the global right to develop, manufacture and commercialize A166, including the right to seek regulatory approvals for A166 in China and all other jurisdictions. In addition, Levena agrees to provide all necessary technical support and assistance throughout the key stages of A166's development, including granting us a global, non-exclusive license, without the right to further grant sublicenses, to utilize certain patents (registered or pending) and know-how related to its linker and payload technologies which are used for A166's development. We take a leading role in, and are primarily responsible for, all key stages of A166's development and commercialization, from preclinical studies, clinical trials, manufacturing, to regulatory approval and commercialization. The intellectual property and know-how arising from A166 Co-development Agreement shall be co-owned by Levena and us. We shall be the patentee and the first inventor of all patents. The second inventor shall be a designated personnel of Levena, and the remaining inventors shall be determined by both parties. As of the Latest Practicable Date, we were the patentee of the four material patents and patent applications relating to A166 as disclosed under "– Intellectual Property."

In consideration of the A166 Co-development Agreement, we agreed to pay Levena license fees up to a total of RMB9.5 million, payable in installments upon the achievement of specified development and regulatory milestones, of which RMB6.5 million had been paid as of the Latest Practicable Date. Upon commercialization, we are also required to pay Levena low single-digit royalties on the annual sales of A166 for a period of ten years after the first commercial sale. Furthermore, either party may seek collaborators to further develop and commercialize A166 outside China and share any economic gains (such as upfront payments, milestone payments and royalties) arising from such overseas collaborations. We are entitled to 65% or 70% of such economic gains, the exact ratio variable based on Levena's efforts in identifying the collaborators.

Any dispute arising from or in connection with the co-development shall be first settled through mutual negotiation between the parties. Where the dispute cannot be successfully settled, it shall be submitted to the designated venue for arbitration.

The A166 Co-development Agreement will remain valid and binding until December 2033, after which the rights granted to us to utilize the patents and know-how related to Levena's linker and payload technologies shall become perpetual and fully paid up. The agreement may be terminated earlier for the following reasons: (i) upon either party's material breach, (ii) we fail to fulfill our payment obligations after Levena's notice, (iii) we determine to terminate the development and commercialization of A166, and (iv) by the parties' agreement upon consultation. If the collaboration is terminated due to Levena's failure to fulfill its contractual obligations, Levena shall refund 50% of any license fees we had paid. In the event of a breach of contract, the defaulting party shall bear all losses incurred by the other party as a result of its breach.

Collaboration and Licensing Agreement with Harbour BioMed for A167

In August 2018, we entered into a strategic collaboration and licensing agreement with Harbour BioMed, under which we granted to Harbour BioMed an exclusive, royalty-bearing, sublicensable license to develop, manufacture and commercialize A167 (also known as "HBM9167" in Harbour BioMed's portfolio), our PD-L1 mAb, outside Greater China (as amended and supplemented, the "A167 Out-license Agreement"). Harbour BioMed, an Independent Third Party, is a biopharmaceutical company engaged in the discovery and development of differentiated antibody therapeutics in immunology and oncology disease areas.

Under the A167 Out-license Agreement, Harbour BioMed was granted the rights to use our patents and know-how relating to A167 to develop, manufacture and commercialize monotherapies or combination therapies based on A167 (the "A167 Licensed Products") outside Greater China, subject to certain rights we have retained to develop combination therapies based on A167 and any agent(s) developed by us or in which we own at least a 50% interest. We also granted Harbour BioMed the right to use such patents and know-how relating to A167 within Greater China for limited purposes, including (i) to facilitate the development and commercialization of the A167 Licensed Products outside Greater China, and (ii) to develop, manufacture and commercialize combination therapies based on A167 and any agent(s) developed, or wholly owned, by Harbour BioMed.

In partial consideration of the A167 Out-license Agreement, Harbour BioMed paid us an upfront payment of US$6.0 million in August 2018. In addition, we are eligible to receive payments upon the achievement of specified development, regulatory and commercial milestones up to US$351.0 million, of which US$2.0 million had been received as of the Latest Practicable Date. We will also be eligible to receive tiered royalties as a high single-digit to low double-digit percentage of the annual net sales of the A167 Licensed Products outside Greater China, subject to certain adjustments, with a royalty term of 15 years commencing upon the first commercial sale of the A167 Licensed Products.

Either party shall own any invention made solely by itself or its agents (including any know-how, data and other information relating to such invention) arising from the performance of the A167 Out-license Agreement and all intellectual property rights therein. Any joint invention shall be co-owned by Harbour BioMed and us, and either party is entitled to utilize such joint invention and to grant non-exclusive licenses based on such invention to third parties. Issuance of exclusive licenses based on joint inventions requires the mutual consent of both parties.

Unless terminated earlier pursuant to its terms, the A167 Out-license Agreement will remain in effect until the expiry of the royalty term. Either party may terminate the A167 Out-license Agreement with a 60 days' prior written notice in the event of (i) the other party's bankruptcy, insolvency or termination of business (other than for the purpose of reorganization or merger), or (ii) the other party's uncured material breach of the A167 Out-license Agreement.

Any disputes arising out of the A167 Out-license Agreement shall be notified by the party raising the dispute to the other party in writing. After receiving such notice, both parties shall schedule a meeting to resolve the dispute. If the dispute cannot be resolved, or such meeting is not held, within a period of time, then the dispute may be submitted to the Hong Kong International Arbitration Centre for final resolution.

See also "Connected Transactions – Non-exempt Continuing Connected Transactions – Licensing Agreement" for details on our patent and technology in-license agreement with Kelun Research Institute, a wholly-owned subsidiary of Kelun Pharmaceutical, in relation to A167, pursuant to which Kelun Research Institute is entitled to a single-digit percentage of the net sales revenue derived from the sale of A167 after its commercialization.

Collaboration and License Agreement with Ellipses for A400

In March 2021, we entered into a collaboration and license agreement with Ellipses, under which we granted to Ellipses an exclusive, royalty-bearing, sublicensable license to develop, manufacture and commercialize A400 (also known as "EP0031" in Ellipses's portfolio), our RET inhibitor, in all countries excluding Greater China, North Korea, South Korea, Singapore, Malaysia and Thailand (collectively, the "Licensed Territory") (as amended and supplemented, the "A400 Out-license Agreement"). Ellipses, an Independent Third Party, is a U.K.-based international drug development company focused on the development of innovative cancer treatments.

Under the A400 Out-license Agreement, Ellipses was granted the rights to use our patents, know-how and other intellectual property rights relating to A400 to develop, manufacture and commercialize products based on A400 (the "A400 Licensed Products") in the Licensed Territory, including the rights to access and use our regulatory submissions and clinical data generated outside the Licensed Territory. We also granted Ellipses a non-exclusive license to use certain of our patents, know-how and other intellectual property rights to manufacture the A400 Licensed Products outside the Licensed Territory, solely for commercializing the A400 Licensed Products in the Licensed Territory. In turn, Ellipses granted to us an exclusive, fully paid-up, sublicensable license to use its patents and know-how outside the Licensed Territory as well as an exclusive license to its clinical data inside the Licensed Territory, solely for the purposes of developing, manufacturing and commercializing the A400 Licensed Products outside the Licensed Territory.

Ellipses and we have established a joint development committee ("JDC") to oversee the development and commercialization of the A400 Licensed Products. We shall, in coordination with Ellipses via the JDC, manage and perform, or procure the performance of, preclinical development activities and experiments as the JDC shall agree are necessary for the IND applications (or any equivalent filings) Ellipses intends to make in the Licensed Territory. Pursuant to A400 Out-license Agreement, if we intend to discontinue or abandon the development or commercialization of A400 or its relevant rights outside the Licensed Territory, Ellipses shall have exclusive first right of refusal, for a period of at least 90 days, in which to acquire any such rights from us.

In consideration of the A400 Out-license Agreement, we are entitled to (i) preclinical development payments up to an aggregate amount of US$2.91 million, payable by installments in accordance with a specified timeline, for our management and oversight of, and costs incurred in, A400's preclinical development activities, including for providing the necessary data and support to facilitate A400's IND filing and maintenance in the Licensed Territory; (ii) technology transfer fee of US$30.0 thousand for furnishing the manufacturing know-how and performing related analysis; (iii) sharing of revenue as low double-digit percentages of the total payments received by Ellipses in consideration for any sub-license agreement(s), if executed; and (iv) tiered royalties as low-teen percentages of the annual net sales of the A400 Licensed Products, on a product-by-product basis, generally with a royalty term of ten years commencing upon the first commercial sale of the A400 Licensed Products in such country or region, subject to adjustments (such as third-party payment offset) as stipulated between the parties. We had received a total of US$3.22 million as of the Latest Practicable Date.

Either party shall own any invention made by itself arising from the performance of the A400 Out-license Agreement and all intellectual property rights therein. A patenting sub-committee has been set up to facilitate discussion and decision-making regarding the applications for intellectual property rights in relation to A400 or the A400 Licensed Products, including to resolve intellectual property-related disputes arising from the collaboration.

Unless terminated earlier in accordance with its terms, the A400 Out-license Agreement will remain in effect until no further payments are due to us, upon which all licenses granted under the agreement shall become perpetual and fully paid-up. Either party may terminate the A400 Out-license Agreement in the event of the other party's uncured material breach, willful misconduct, fraud, breach of anti-bribery obligations, or gross negligence in relation to its obligation under the agreement. We are also entitled to termination of the A400 Out-license Agreement upon written notice to Ellipses in the event of (i) Ellipses's failure to exercise commercially reasonable efforts to conduct clinical activities in a timely manner as contemplated by the agreement, unless excusable under specific circumstances, or (ii) Ellipses's insolvency (other than for the purpose of reorganization or merger), asset possession by competent authorities or persons or likewise.

The JDC facilitates communications between the parties to discuss and perform the development plan. The JDC will endeavor to make decisions by consensus. If the dispute or failure to agree cannot be resolved by the JDC, Ellipses shall generally have the casting vote in respect of such decision to the extent it applies inside the Licensed Territory, and we shall generally have the casting vote in respect of such decision to the extent it applies outside the Licensed Territory. The patenting sub-committee of the JDC will coordinate the filing of patent applications and other matters related to intellectual property, and endeavor to resolve disputes arising therefrom.

Cooperative Development Agreement with Harbour BioMed for SKB378

In May 2019, we entered into a cooperative development agreement with Harbour BioMed (Suzhou) Co., Ltd. (recently renamed NONA BIOSCIENCES (SUZHOU) CO., LTD.), an indirect wholly owned subsidiary of Harbour BioMed, to jointly develop SKB378 (also known as "HBM9378" in Harbour BioMed's portfolio), our anti-TSLP mAb, utilizing Harbour BioMed's H2L2 antibody platform and related know-how (as amended and supplemented, the "SKB378 Co-development Agreement").

Under the SKB378 Co-development Agreement, at the drug discovery and development stage, Harbour BioMed and we each assume certain responsibilities in SKB378's preclinical and clinical studies, as well as regulatory affairs, pursuant to a co-development plan agreed between the parties. Both parties take an active role in advancing SKB378's global clinical development plan. Harbour BioMed is primarily responsible for seeking IND approval and conducting clinical trials for SKB378 in Greater China, North America and certain Asia-Pacific countries, while we carry out the same responsibilities in all other countries and regions, including the E.U. The parties equally share all costs related to SKB378's clinical development plans across territories, including expenses associated with the application for IND and marketing approvals in the respective jurisdiction.

Harbour BioMed and we have established a joint development committee ("JDC") to oversee the development and commercialization of SKB378. As SKB378 approaches commercialization, Harbour BioMed shall take a leading role in seeking and obtaining marketing approvals for SKB378 in North America and certain Asia-Pacific countries (excluding Greater China), while we shall take a leading role in doing so in all other countries and regions, including Greater China and the E.U. Each party is obligated to provide the necessary support and assistance, as reasonably requested by the other party, to facilitate the requisite regulatory submissions and communications. Subject to certain adjustments under limited circumstances, the parties equally share all net profits arising from SKB378's future commercial sales within the term of the SKB378 Co-development Agreement.

Harbour BioMed granted us a license to use certain of its background intellectual property rights, including know-how related to its H2L2 antibody platform, to enable SKB378's joint development. Any intellectual property and know-how arising from the collaboration under the SKB378 Co-development Agreement shall be co-owned by Harbour BioMed and us. Either party is entitled to utilize intellectual property rights related to A378 to develop derivative products or combination therapies upon notifying the other party.

In partial consideration of the SKB378 Co-development Agreement, Harbour BioMed agreed to reimburse us for certain discovery and preclinical R&D activities. In turn, we agreed to reimburse Harbour BioMed for certain costs it incurred in relation to SKB378's IND application and clinical studies in Greater China, payable upon the achievement of specified clinical development and regulatory milestones in Greater China.

Either party is entitled to terminate the SKB378 Co-development Agreement under certain circumstances, including: (i) upon written agreement by the parties, (ii) with a 30 days' prior written notice in the event of the other party's uncured material breach, and (iii) material delays or significant decline of asset value due to technical feasibility issues which cannot be resolved by the parties. If one party chooses to opt out of SKB378's co-development plan in specific region(s), upon or before the termination of the SKB378 Co-development Agreement, the remaining party is entitled to assume all rights previously granted to the departing party within the respective region(s), subject to certain conditions and provided that the departing party is reimbursed in accordance with the relevant financial terms.

The JDC will endeavor to make decisions by consensus. If a dispute or failure to agree arises which cannot be resolved by the JDC, the chairman of the board or chief executive officer of each party shall confer in a timely manner. In the event the designated representatives are unable to resolve the issue, then Harbour BioMed shall generally have the final decision-making authority with respect to the matters pertaining to North America and certain Asia-Pacific countries (excluding Greater China), while we shall have the final decision-making authority with respect to all matters pertaining to all other countries and regions, including Greater China and the E.U.

MANUFACTURING

To date, our manufacturing activities are primarily limited to supporting our drug development process. For more details, see "– Research and Development – R&D Facilities." Anticipating future commercialization, we are building up our own cGMP-compliant pilot-scale and commercial-scale manufacturing capabilities to ensure delivery of high-quality drug products. We also engaged, and will continue to engage, industry-recognized CMOs to supplement our in-house capacity so as to enhance efficiency and reduce operational and regulatory compliance costs.

Manufacturing Facilities

Our manufacturing facilities are designed to meet the manufacturing challenges associated with the production of complex molecules such as ADCs, which require integrated manufacturing capabilities that span across biologics and small molecules, and a dedicated manufacturing environment that allows the safe manipulation of highly active agents. Our manufacturing facilities are designed in compliance with the NMPA and FDA's regulatory requirements and cGMP standards in China, the U.S. and Europe. As of December 31, 2022, our manufacturing team consisted of over 180 employees.

Our main manufacturing site in Chengdu has a total floor area of over 10,600 m^2, including approximately 9,400 m^2 designated for commercial-scale production. See "– Properties." It is one of the few facilities in China with cGMP-compliant, end-to-end capabilities covering the entire development lifecycle of ADCs from cell culture and purification, antibody production, syntheses of payloads and linkers, ADC conjugation to formulation, fill and finish.

Our existing commercial-scale manufacturing facilities mainly consist of: (i) cell culture and purification facilities equipped with two 2,000 L single-use bioreactors; (ii) antibody formulation facilities equipped with annual production capacity to produce 60 batches (or 750,000 vials) of freeze-dried formulation or 100 batches (or 2.6 million vials) of injectable solutions; (iii) payload-linker synthesis facilities with annual production capacity of 15 batches; (iv) ADC conjugation facilities equipped with one 300 L ADC conjugation tank with a maximum annual production capacity of 40 batches of ADC drug substance; and (v) ADC formulation facilities with annual production capacity of 45 batches (or 900,000 vials) of freeze-dried ADCs or 60 batches (or 1.2 million vials) of injectable ADCs.

We have set up a professional manufacturing team with management personnel with decades of work experience in leading pharmaceutical companies, such as Eli Lilly, BMS and Akeso. We are also training up young talents to enhance our in-house technical capabilities. In anticipation of the increased demand upon commercialization, we are actively evaluating the addition of new manufacturing facilities and the expansion of existing manufacturing facilities. For our cell culture and purification unit, we plan to install one additional 2,000 L single-use bioreactor, bringing our total in-house capacity to 6,000 L. Going forward, we will continue to enhance our manufacturing capabilities to ensure that we have sufficient capacity for our commerical-scale production. See also "Future Plans and [**REDACTED**]."

CMOs

We currently outsource certain manufacturing activities, primarily the production of small molecules, to industry-recognized CMOs in China, and we intend to continue doing so in the future. We believe it is cost-effective and efficient to engage CMOs for certain manufacturing activities as it reduces the capital expenditure required for setting up and maintaining the necessary production lines, and allows us to focus on the core processes of ADC manufacturing.

We select CMOs by taking into account a number of factors, such as their manufacturing capacity and qualifications, geographic proximity and track record, applicable regulations and guidelines, as well as our R&D objectives and the specifications set by our collaborators. To monitor and evaluate the services of our CMOs, we conduct quality assurance audit programs to ensure, among other criteria, full compliance of our CMOs with the relevant regulatory requirements.

Following a rigorous consultation and bidding process, we enter into formal agreements with the selected CMOs. Key terms of our agreements that we typically enter into with our CMOs are set forth below.

- ***Services***. The CRO provides us with manufacturing services according to the types of deliverables, location, unit price, volume and requested delivery date specified by us.

- ***Quality control and inspections***. We are entitled to conduct on-site audits and regular inspections to ensure compliance of our CMOs with the relevant cGMP and regulatory requirements.

- ***Payments***. We are required to make payments to the CMOs in accordance with the payments schedule set forth in the agreement, which is typically linked to the stages of the manufacturing process and the deliverables we receive.

- ***Intellectual property rights***. We own all intellectual property rights arising from the outsourced manufacturing processes.

- ***Remedies for non-conforming products***. We are entitled to remedies for products that fail to conform to our specifications. The CMOs are required to replace the non-conforming products and compensate us for any direct losses due to the delay.

For risks relating to CMOs, see "Risk Factors – Risks Relating to Dependence on Third Parties – We may rely on third parties to manufacture our drug products for clinical development and commercial sales. Our business could be harmed if these third parties fail to deliver sufficient quantities of product or fail to do so at acceptable quality or price levels."

QUALITY CONTROL

We operate a comprehensive quality control system which extends across all key stages of the R&D, manufacturing and commercialization processes. This system is established and refined in accordance with the rigorous regulations and guidelines in China, the U.S. and Europe. We pay close attention to the evolving cGMP standards and regulatory developments in these target markets and update our internal procedures accordingly, striving for the highest international standards in patient safety and regulatory compliance. Furthermore, our quality expert team are actively involved in the discussion and promulgation of regulations and guidelines in China, which attests to our recognized expertise in the respective fields. For example, we took an active role in the drafting of the "Biological Products (mAb)" section of the Chinese GMP Implementation Guide (Re-issued) (中國GMP實施指南(再版)《生物製品(單克隆抗體)》部分) in 2022.

As of December 31, 2022, our quality management team comprised over 150 members, including 136 overseeing our manufacturing process and 17 overseeing our preclinical studies and clinical trials. They oversee the quality systems covering all key stages of our drug development process, from R&D, manufacturing to commercialization, including discovery, preclinical research and discovery, clinical trials, procurement, supply chain, process development, production, warehousing, delivery and recalls.

We have established comprehensive quality control and quality assurance procedures to ensure that our manufacturing processes comply with relevant regulatory requirements and our internal quality standards. We select qualified raw material suppliers, and recruit manufacturing and quality management personnel based on a strict set of criteria. We regularly inspect our facilities and equipment to ensure that our processes, methods, programs and equipment function properly. We closely monitor the manufacturing environment, especially key parameters such as microbial levels, temperature, and humidity. We generally perform overall inspections every year and engage external experts and counsel to conduct quality audit. We strive to upgrade and improve our comprehensive quality control system, benchmarking against the highest international standards adopted by pharmaceutical MNCs, to ensure patient safety and regulatory compliance.

COMMERCIALIZATION

We are well-positioned to develop our commercialization infrastructure and market access, leveraging our Controlling Shareholder Kelun Pharmaceutical's decades-long experience, industry connections and extensive network. Guided by Kelun Pharmaceutical's leading industry position, strong brand image and profound resources as one of China's largest and most established pharmaceutical companies, we are planning to develop our own commercialization team and network, with an initial focus on Class III hospitals and leading physicians across China's extensive local markets. We will also continue to refine our commercialization strategies for each late-stage drug candidate, first prioritizing therapeutic areas with medical needs in China, such as BC, NSCLC and GI cancers, while offering synergistic treatment options enabled by our diverse pipeline to optimize patient outcome.

Based on the expected approval timeline of each late-stage project in our pipeline, we expect to receive conditional marketing approval from the NMPA for A167 (PD-L1 mAb), our first innovative drug in NDA registration stage, in the second half of 2023 or the first half of 2024. Subject to regulatory communications and marketing approval, we expect to launch our Core Products, SKB264 and A166, and A140 in the China market in the second half of 2024 or the first half of 2025. In anticipation of these upcoming milestones, we are actively recruiting talent with a strong background in oncology, especially in BC, NSCLC, GI cancers and NPC, our lead indications for these late-stage assets. We plan to set up a fully-fledged commercialization team by the end of 2023 to oversee and coordinate the sales and marketing of A167, as well as the pre-marketing preparation for SKB264 and A166, laying the groundwork for rapid commercial-scale distribution upon these two ADCs' anticipated NDA approval by the NMPA. Globally, we will continue to pursue a flexible strategy to capture the commercial value in major international markets, through forging synergistic license and collaboration opportunities worldwide.

BUSINESS DEVELOPMENT

We have established robust, cross-border business development capabilities with local presence across multiple jurisdictions, from Chengdu, Beijing and Shanghai in China to New Jersey in the U.S. Our business development team is led by seasoned professionals with decades-long experience and insights in sourcing and executing licensing deals and collaborations. They work closely with our scientists and team leaders on each project, and are involved as early as the drug discovery stage to identify and capture partnership opportunities.

Our business development competencies are exemplified by a proven track record in forging strategic partnerships worldwide, which in turn reflect the increasing recognition we have received from peers and leaders in the global biopharmaceutical industry. Notably, we have successfully negotiated nine out-license agreements to date, including three license and collaboration agreements with MSD to develop up to nine ADC assets for cancer treatment. According to Frost & Sullivan, we are the first China-based company to license internally discovered and developed ADC candidates to a top-ten biopharmaceutical MNC. Our collaboration with MSD to develop up to seven preclinical ADC assets is the largest biopharmaceutical out-license deal to date secured by a China-based company, according to Frost & Sullivan, and the world's largest biopharmaceutical partnership in terms of deal value in 2022, according to Nature Reviews Drug Discovery. We have also entered into collaboration and license agreements with Ellipses for A400, and with Harbour BioMed for A167 and SKB378. Our strategic partnerships are not only testaments to our R&D and business development capabilities, but also key drivers of our continued innovation, global influence and long-term growth. See also "– Our Development Strategies – Continue to seek and deepen strategic partnerships to extend the potential of our technology platforms and maximize the value of our pipeline."

INTELLECTUAL PROPERTY

Intellectual property rights are important to the success of our business, and we are committed to the development and protection of our intellectual properties. Our future commercial success depends, in part, on our ability to obtain and maintain patent and other intellectual property and proprietary protections for commercially important technologies, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid, enforceable intellectual property rights of third parties.

We have a global portfolio of patents to protect our drug candidates and technologies. As of the Latest Practicable Date, we owned (i) 74 issued patents in China, (ii) 21 issued patents in the U.S., (iii) 52 issued patents in other jurisdictions, and (iv) 255 pending patent applications, including 100 in China, 14 in the U.S., 16 under the Patent Cooperation Treaty (PCT) and 125 in other jurisdictions. The patents granted to, or under application by, our Company cover all material aspects of our Core Products.

As of the Latest Practicable Date, with respect to our two Core Products, SKB264 and A166, we owned five issued patents in China and eight issued patents in other jurisdictions, as well as 21 pending patent applications, including six in China, five in the U.S., three under the PCT and eight in other jurisdictions. With these patents, we own both SKB264 and A166 as differentiated drug molecules as these patents comprehensively cover their structure, formulation, method of preparation and use.

The following table summarizes the details of the material granted patents and patent applications in connection with our Core Products. For details, please see "Appendix VII – Statutory and General Information – Further Information About our Business – 2. Our Intellectual Property Rights - (b) Patents."

Related Product	Scope of Patent Protection	Category	Patent Number/ Patent Application Number	Jurisdiction	Patent Holder/ Applicant	Expiration Year*
SKB264	Camptothecin derivatives and their water-soluble prodrugs, pharmaceutical compositions containing them, their preparation methods and uses	Invention	2020800065387	China	Our Company	N/A**
SKB264	Biologically active substance conjugate and its preparation method and use	Invention	2018800695435	China	Our Company	2038
		Invention	US16758980	U.S.	Our Company	N/A**
SKB264	Use of medicament in treatment of tumor disease	Invention	WO2022228497A1	PCT	Our Company	N/A**
A166	Anti-ErbB2 antibody-drug conjugate and its composition, preparation method and application	Invention	2015108240648	China	Our Company	2035
A166	Anti-ErbB2 antibody-drug conjugate and its composition, preparation method and application	Invention	2016800367605	China	Our Company	2036

Related Product	Scope of Patent Protection	Category	Patent Number/ Patent Application Number	Jurisdiction	Patent Holder/ Applicant	Expiration Year*
A166	Use of anti-HER2 antibody-drug conjugates in the treatment of cancer	Invention	2019800186355	China	Our Company	N/A**
A166	Anti-ErbB2 antibody-drug conjugate and its composition, preparation method and application	Invention	JP2017566133	Japan	Our Company	2036

* Patent expiration does not include any applicable patent term extensions

** Pending patent application.

As of the Latest Practicable Date, we owned two issued Chinese utility model patents for our various innovative technologies that are utilized throughout our drug development and manufacturing process, including (i) a device for detecting oxygen level in ampules (No. 2019214180811) and (ii) a buffer preparation system (No. 202121433214X). These utility model patents have a term of ten years from the date of filing and are expected to expire in and after 2029.

The actual protection afforded by a patent varies on a claim-by-claim and jurisdiction-by-jurisdiction basis and depends upon many factors, including the type of patent, the scope of its coverage, the availability of any patent term extensions or adjustments, the availability of legal remedies in a particular jurisdiction and the validity and enforceability of the patent. We cannot provide any assurance that patents will issue with respect to any of our owned or licensed pending patent applications or any such patent applications that may be filed in the future, nor can we provide any assurance that any of our owned or licensed issued patents or any such patents that may be issued in the future will be commercially useful in protecting our drug candidates and methods of manufacturing the same. See "Risk Factors – Risks Relating to Our Intellectual Property Rights" for a description of risks related to our intellectual property.

We conduct our business under the brand name of "Kelun Biotech" ("科伦博泰"). As of the Latest Practicable Date, we had registered 59 trademarks in China and 59 trademarks in other jurisdictions. We are also the registered owner of one domain name.

We enter into license and collaboration agreements and other relationships with biopharmaceutical companies and other industry participants, through which we may grant access to our own intellectual property, or gain access to the intellectual property of others. See "– Our License and Collaboration Arrangements."

During the Track Record Period and up to the Latest Practicable Date, we had not been 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.

See "Appendix VII – Statutory and General Information – B. Further Information about Our Business – 2. Our Intellectual Property Rights" to this document for further information.

SUPPLIERS AND PROCUREMENT

During the Track Record Period, our suppliers primarily consisted of (i) suppliers of raw materials and consumables for our drug development, (ii) suppliers of equipment and devices for our manufacturing activities and construction service providers for our new facilities, and (iii) CROs, who provide third-party contracting services for research and development.

A majority of our raw materials are widely available, and we are able to purchase them from numerous suppliers around the world according to our product development plans. The raw materials procured for our product candidates primarily include cell culture media, chromatography resins, excipients, packaging materials, nanofiltration and ultrafiltration membranes, bioreactor and single-use bioprocess bags and other ancillary materials used for our research and development activities. We have established stable collaboration relationships with qualified suppliers for raw materials, which we believe have sufficient capacity to meet our demands. Nevertheless, we believe that adequate alternative sources for such supplies exist. To monitor the quality of supplies, we implemented a standardized operating system, setting out the procedures and guidelines for the procurement of raw materials, quality control inspection, warehousing, testing, and storage. In particular, for overseas suppliers, we typically devise a comprehensive procurement plan in advance to ensure sufficient and timely supply. A number of our overseas suppliers have established local branches or subsidiaries in China, which provides more convenience and visibility for our procurement. Meanwhile, we are exploring collaboration opportunities with alternative domestic suppliers, such as for the supply of cell culture media. During the Track Record Period, we did not experience any material shortage or delays in the supply of raw materials.

See also "– Research and Development – Collaboration with CROs" for details on our relationship with the CROs.

For the years ended December 31, 2021 and 2022, our purchases from our largest supplier accounted for 24.4% and 12.0% of our total purchases and our purchases from our five largest suppliers in the aggregate accounted for 48.4% and 38.9% of our total purchases, respectively. During each year of the Track Record Period, Kelun Group (together with Kelun Medicine & Trade Group), was our largest supplier. For further details, please see "Connected Transactions." The following table sets forth details of our five largest suppliers during the Track Record Period.

Supplier	Background	Products/ services provided	Commencement of business relationship	Credit terms	Purchase amount *(RMB in thousands)*	% of total purchases
For the year ended December 31, 2021						
Supplier A	Kelun Group together with Kelun Medicine & Trade Group	R&D service, sales of materials and equipment	2018	N/A*	187,881	24.4%
Supplier B	A China-based company primarily engaged in construction and engineering	Construction	2020	14 days	96,092	12.5%
Supplier C	A China-based company together with its related parties, primarily engaged in sales of pharmaceuticals, technology promotion and application services	R&D service	2020	30 days	37,910	4.9%
Supplier D	A China-based company primarily engaged in wholesale and retail of pharmaceuticals and inspection services	R&D service	2018	15 days	29,116	3.8%
Supplier E	A China-based company primarily engaged in construction and engineering	Construction	2021	14 days	21,983	2.9%
Total					**372,982**	**48.4%**

Supplier	Background	Products/ services provided	Commencement of business relationship	Credit terms	Purchase amount *(RMB in thousands)*	% of total purchases
For the year ended December 31, 2022						
Supplier A	Kelun Group together with Kelun Medicine & Trade Group	R&D service, sales of materials and equipment	2018	N/A[(1)]	129,913	12.0%
Supplier C	A China-based company together with its related parties, primarily engaged in sales of pharmaceuticals, technology promotion and application services	R&D service	2020	30 days	120,827	11.1%
Supplier F	A China-based company together with its related parties, primarily engaged in pharmaceutical production, wholesale and retail of pharmaceuticals and inspection services	R&D service	2022	30 days	75,070	6.9%
Supplier B	A China-based company primarily engaged in construction and engineering	Construction	2020	14 days	54,808	5.0%

Supplier	Background	Products/ services provided	Commencement of business relationship	Credit terms	Purchase amount *(RMB in thousands)*	% of total purchases
Supplier G	A China-based company together with its related parties, primarily engaged in sales of pharmaceuticals, technology promotion and application services	R&D service	2021	30 days	41,568	3.8%
Total					**422,186**	**38.9%**

Note:

(1) Credit terms are not specified under the relevant contracts.

To the best of our knowledge, except for Kelun Group (together with Kelun Medicine & Trade Group), (i) all of our five largest suppliers during the Track Record Period are independent third parties, and (ii) none of our Directors, their respective associates or any shareholder who owned more than 5% of our issued share capital as of the Latest Practicable Date has any interest in any of our five largest suppliers during the Track Record Period. Kelun Group (together with Kelun Medicine & Trade Group) was also among our five largest customers during the Track Record Period. See also "Financial Information – Material Related Party Transactions."

CUSTOMERS

During the Track Record Period, our revenue was primarily derived from (i) our license and collaboration agreements with MSD and other licensing partners, and (ii) provision of research and development services to Kelun Group and other third parties. For further details, please see "Financial Information – Description of Selected Components of the Consolidated Statements of Profit or Loss and Other Comprehensive Income – Revenue."

For the years ended December 31, 2021 and 2022, our revenue generated from our largest customer accounted for 61.6% and 90.8% of our total revenue, and revenue from our five largest customers in the aggregate represented over 99.9% of our total revenue in each year. During each year of the Track Record Period, Kelun Group (together with Kelun Medicine & Trade Group) was one of our largest customers. The following table sets forth details of our five largest customers during the Track Record Period.

Customer	Background	Services	Commencement of business relationship	Credit terms	Revenue contribution *(RMB in thousands)*	% of total revenue
For the year ended December 31, 2021						
Customer A	Kelun Group together with Kelun Medicine & Trade Group	R&D services	2018	N/A*	19,919	61.6%
Customer B	A European company primarily engaged in innovative drug development	License and collaboration	2020	30 days	11,937	36.9%
Customer C	A China-based company together with its related parties, primarily engaged in drug development and production	R&D services	2021	10 days	328	1.0%
Customer D	A China-based company primarily engaged in the development of innovative drugs	R&D services	2021	10 days	138	0.4%
Total					32,322	100.0%
For the year ended December 31, 2022						
Customer E	A US-based company primarily engaged in the development of innovative health solutions	License and collaboration	2021	45 days	730,037	90.8%
Customer A	Kelun Group together with Kelun Medicine & Trade Group	R&D services	2018	N/A(1)	55,950	7.0%
Customer F	A European company primarily engaged in innovative drug development	License and collaboration	2017	30 days	12,749	1.6%
Customer B	A European company primarily engaged in drug development	License and collaboration	2020	30 days	4,659	0.6%

Customer	Background	Services	Commencement of business relationship	Credit terms	Revenue contribution *(RMB in thousands)*	% of total revenue
Customer C	A China-based company together with its related parties, primarily engaged in drug development and production	R&D services	2021	10 days	396	0.0%
Total					803,791	100.0%

Note:

(1) Credit terms are not specified under the relevant contracts.

To the knowledge of our Directors, except for Kelun Group (together with Kelun Medicine & Trade Group) and MSD, none of our Directors, their respective associates or any shareholder who owned more than 5% of our issued share capital as of the Latest Practicable Date has any interest in any of our five largest customers during the Track Record Period.

COMPETITION

Our industry is highly competitive and subject to rapid and significant change. While we believe that our innovative technology platforms, our drug candidates in both oncology and non-oncology therapeutic areas, and our experienced leadership team provide us with competitive advantages, we face potential competition from many others working to develop therapies targeting the same indications. These include major biopharmaceutical companies, specialty pharmaceutical and biotechnology companies, and academic institutions, government agencies and research institutions. Any drug candidates that we successfully develop and commercialize will compete both with existing drugs and with any new drugs that may become available in the future. For more information on the competitive landscape of our drug candidates, please refer the paragraph headed "– Our Pipeline" and "Industry Overview."

EMPLOYEES

As of December 31, 2022, we had 1,155 full-time employees, substantially all of whom were based in China. The following table sets forth the details of our employees by function:

Function	Number	% of Total
Research and development*	766	66.3%
Manufacturing and quality control	325	28.1%
Senior management	6	0.5%
General and administrative	58	5.0%
Total	**1,155**	**100.0%**

* Including 17 quality control personnel staffed within our research and development team, who were responsible for quality control in our preclinical studies and clinical trials.

We recruit our employees primarily through online platforms, recruiting websites, headhunter referral and job fairs. We conduct induction programs and periodic professional training for all employees.

We enter into individual employment contracts with our employees covering matters such as salaries, bonuses, employee benefits, workplace safety, confidentiality obligations, work product assignment clause and grounds for termination. The remuneration package of our employees includes salary and bonus, which are generally determined by their qualifications, performance review, and seniority. We also offer share incentives and promotion opportunities to motivate our employees. See also "Risk Factors – Risks Relating to Our Operations – We may be subject to additional social insurance fund and housing provident fund contributions and late fees or fines imposed by relevant regulatory authorities."

We also enter into separate confidentiality agreements, which contain non-competition clauses, with our senior management and certain key members of our R&D team and other employees who have access to trade secrets or confidential information about our business and may be considered possible, directly or indirectly, to compete with us.

As of the Latest Practicable Date, all of our employees were members of our labor union. During the Track Record Period and up to 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. Our existing insurance policies cover adverse events in our clinical trials, group life insurance, public liability insurance, environmental pollution liability insurance, and general insurance for properties and machinery damage. 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. We believe our existing insurance coverage is adequate for our present operations and in line with the industry practice in the PRC. See also "Risk Factors – Risks Relating to Our Operations – We have limited insurance coverage, and any claims beyond our insurance coverage may result in our incurring substantial costs and a diversion of resources."

SOCIAL, HEALTH, WORK SAFETY AND ENVIRONMENTAL MATTERS

We believe our long-term success rests on our ability to make positive impact on the society. As our business continues to grow, we will adhere to our mission to address major medical needs in China and globally, and to bring world-class treatments, and a healthier and happier life, to all patients.

Governance on ESG Matters

We are committed to social responsibilities and consider environmental, social and governance ("**ESG**") essential to our continuous development. Our Board is responsible for overseeing and guiding our ESG initiatives and setting our ESG strategies and policies. Our Environment, Health and Safety ("**EHS**") working group is responsible for monitoring the day-to-day practice of ESG-related matters and implementing our ESG policies. We have also set up a dedicated ESG working team, which report to our Board and management team and are responsible for executing the ESG strategies and targets set by the Board.

Our Board is currently in the process of adopting a comprehensive ESG policy (the "**ESG Policy**") in accordance with the Listing Rules, which will set forth our corporate social responsibility objectives, including (i) the appropriate risk governance on ESG matters; (ii) identification of key stakeholders and the communication channels to engage with them; (iii) our ESG governance structure; (iv) our ESG strategy formation procedures; (v) our ESG risk management and monitoring; and (vi) the identification of key performance indicators and mitigating measures.

We believe our continued growth rests on integrating social values into our business. We are setting up an ESG committee, which will be led and supervised by our management and be responsible for establishing, adopting and reviewing our ESG Policy. The key duties and responsibilities of our ESG committee include:

- keeping abreast of the latest ESG-related laws and regulations, including the applicable sections of the Listing Rules, keeping our management informed of any changes in such laws and regulations, and updating our ESG Policy in accordance with the latest regulatory updates;

- identifying our key stakeholders based on our business operations and understanding such stakeholders' influences with respect to ESG matters;

- assessing ESG-related risks on a regular basis to ensure we fulfill our responsibilities with respect to ESG matters;

- ensuring and continuously monitoring the implementation of our ESG Policy and periodically reviewing the effectiveness of our ESG Policy; and

- reporting to our management on an regular basis on the implementation of our ESG Policy and preparing periodic ESG reports.

Environmental Protection

We strive to operate our facilities in a manner that protects the environment. During the Track Record Period and up to the Latest Practicable Date, we had been in compliance with environmental laws and regulations applicable to our operations in all material respects and there had been no material claim or penalty imposed on us as a result of a violation of environmental laws and regulations that would materially and adversely affect our business, financial condition or results of operations. For the year ended December 31, 2021 and 2022, our expenses in relation to environmental compliance matters were RMB668.2 thousand and RMB771.1 thousand, respectively.

Climate-related risks

The environmental and climate-related risks we are exposed to can be divided into two broad categories: physical and transition risks. We define physical risks as risks related to the physical impacts of climate change, consisting of 1) acute physical risks, such as increased severity of typhoon or floods; and 2) chronic physical risks that are affected by long-term changes in climate patterns, such as changes in average annual rainfall or temperature. We define transition risks as the transition from dependence on fossil fuels to a low-carbon economy, which may involve changes in policy, laws, technology markets, as well as social culture, such as possible carbon taxes, compliance disclosures, and increased use of new energy sources across businesses and households. Potential risks to premises, operations, supply chains, transportation needs, and employee safety also impact our finances.

Our ESH working group closely monitors climate change policies to reduce the possible impacts of physical and transition risks. We incorporate environmental risk analysis into the risk assessment process and risk preference setting. If risks and opportunities are deemed material, we incorporate them into our strategic and financial planning processes and take appropriate mitigation measures.

Our business, operations and financial condition had not been materially affected by any climate-related events during the Track Record Period and up to the Latest Practicable Date.

Energy

We actively explore strategies to reduce energy consumption, primarily electricity consumption. For instance, we actively promote energy conservation and consumption reduction in our daily operations. We encourage the purchase and use of energy-efficient electronic equipment in our office premises, including the choice of lighting and other electrical appliances used. Our employees are reminded to ensure that the air conditioning and other power-consuming equipment at our office premises are switched off when they are not in use.

Water Resources

We focus on water resources issue and actively shoulder the social responsibility of protecting water resources. Municipal water supply networks are the main incoming source of our Company's water, and we did not encounter major difficulties seeking suitable water sources during the Track Record Period. Since we have not yet started commercial-scale production, our water resources are mainly used for daily use in offices, laboratories and manufacturing facilities to support our in-house research and development activities, and certain construction projects during the Track Record Period.

Emissions

Waste

We have procedures in place for waste management to ensure compliant waste disposal and reduce environmental impact. The waste we produce is divided into hazardous waste (such as chemical waste and liquid) and non-hazardous waste (such as domestic waste from general office operations). The wastewater and solid waste generated in our in-house research and development process are pretreated by us before being processed by qualified third-party medical waste treatment companies. We use natural gas boilers with low-nitrogen combustion technology, which can significantly reduce emissions of particulates, sulfur dioxide and nitrogen oxide.

Greenhouse gas emission

Our greenhouse gas emissions consist of Scope 1 and Scope 2 emissions. Scope 1 direct emissions include the greenhouse gas emissions from our manufacturing facilities and other stationary combustion sources. Scope 2 energy indirect emissions primarily include the greenhouse gas emissions from our usage of purchased electricity. In response to the national target of carbon neutrality, we actively focus on reducing the greenhouse gas emissions generated during our operations.

We rely on various metrics to measure the impact of environmental risks, which are broadly aligned with industry standards. Such metrics include the number of resource consumption, amount of wastewater generated and the amount of hazardous waste generated. We have also set various goals to reduce our environmental impacts, and we continue to take significant steps toward these targets. The following table sets forth our resource use and emission related indicators during the Track Record Period.

	For the years ended December 31,	
	2021	**2022**
Energy consumption		
Electricity (MWh)	12,281	16,132
Water (tons)	181,073	250,249
Emission		
Exhaust gas (million cubic meters)	37	58
Hazardous waste (tons)	74	104
Greenhouse gas emissions (tons of CO_2 equivalent)	8,694	14,143
– Scope 1 (direct emissions) (tons of CO_2 equivalent)	278	4,585
– Scope 2 (indirect emissions) (tons of CO_2 equivalent)	8,416	9,558

With the expansion of our business and anticipated commercialization of our drug candidates, we expect our resource consumption and emissions to increase. However, we will continue to adopt a wide range of measures, including to strengthen source control, implements cleaner production, rationally utilize resources, conscientiously and responsibly treat laboratory waste and water discharge, and reduce pollution in the whole process. At the same time, we strive to cultivate a corporate culture of environmental protection and work closely with our business partners to build an environment-friendly ecosystem. We are committed to improving the environmental performance of our entire value chain, including office operations, supplier selection, raw material inflow, laboratory experiments, manufacturing process and waste management. In 2023, we aim to control our energy consumption level at approximately 90% to 120% of that recorded in 2022.

Work Safety

We are committed to providing a safe working environment for our employees, as we believe a safe and health workplace is not only important for the well-being of our employees, but also essential to the sustainability of our business. We have implemented rigorous company-wide work safety guidelines and host regular safety training programs to ensure that all of our employees are equipped with the necessary awareness and technical know-how to perform their work in a safe and effective manner. We conduct regular safety inspections for

our laboratories and manufacturing facilities to assist responsible employees in identifying and rectifying potential health and safety hazards. As an integral part of work safety and quality assurance, we also perform routine maintenance to ensure that all equipment in the laboratories and manufacturing facilities are safe for use, including by identifying and repairing faulty equipment and equipment parts. Since our operations involve the use of hazardous materials, we have implemented safety protocols that set out guidelines on potential safety hazards and procedures for operating in the laboratory and manufacturing facilities, including but not limited to the handling, use, storage, treatment and disposal of hazardous materials, as well as emergency planning and response. During the Track Record Period and up to the Latest Practicable Date, we did not have any major workplace accidents.

Workplace Diversity

Within our organization, we are committed to creating an open and inclusive workplace that promotes equality. We hire employees based on their merits and it is our corporate policy to offer equal opportunities to them regardless of gender, age, race, religion or any other social or personal characteristics. As of December 31, 2022, more than 60% of our total employees were female. We adhere to a fair and transparent employee management system and strive to enhance gender and age diversity of our workforce.

Going forward, intend to actively identify and monitor the actual and potential impact of ESG-related risks on our business, strategy and financial performance and incorporate considerations for ESG issues into our business, strategic and financial planning, in compliance with the recommendation of the Environmental, Social and Governance Reporting Guide in Appendix 27 to the Listing Rules.

PROPERTIES

Owned Properties

Our headquarters are located in Chengdu, Sichuan, China. As of the Latest Practicable Date, we owned land use rights to two parcels of land in the PRC, with an aggregate site area of approximately 132,341.8 m^2. We hold the valid title for these parcels of land.

Leased Properties

As of the Latest Practicable Date, we leased 16 properties for production and office use in China, with an aggregate GFA of approximately 36,411.0 m^2, eight of which were leased from Kelun Group. The following table sets forth the details of our leased properties as of the Latest Practicable Date.

Lessor	Location	GFA (m^2)	Expiration Date	Usage
Kelun Group	Chengdu, Sichuan, China	25,386.61	December 31, 2024	Manufacturing
		207.65	December 31, 2024	Warehouse
		38.76	December 31, 2024	Warehouse
		1,308.4	December 31, 2024	Office
		3,264.72	December 31, 2024	Manufacturing
		3,461.34 in total	December 31, 2024	Residential
		1,455.89 in total	December 31, 2024	Residential
		176.56	December 31, 2024	Residential
Third Party Lessor	Guangzhou, Guandong, China	150.6	July 14, 2023	Office
Third Party Lessor	Hefei, An'hui, China	84.8	March 17, 2024	Office
Third Party Lessor	Xi'an, Shan'xi, China	122.86	July 25, 2024	Office
Third Party Lessor	Shenyang, Liaoning, China	142.72	March 26, 2024	Office
Third Party Lessor	Shanghai, China	61.89	July 8, 2024	Residential
Third Party Lessor	Wuhan, Hubei, China	94.78	April 30, 2026	Office
Third Party Lessor	Guangzhou, Guangdong, China	328.60	March 29, 2026	Office
Third Party Lessor	Changsha, Hunan, China	124.77	February 13, 2024	Office

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	Year Granted	Granting Authority
National Engineering Research Center of Targeted Biologics (生物靶向藥物國家工程研究中心)	2022	NDRC
Innovation and Experiment Center for Postdoctoral Fellows (博士後創新實踐基地)	2021	Human Resources and Social Security Department of Sichuan Province
National High-Tech Enterprise (國家高新技術企業)	2020	Department of Science and Technology of Sichuan Province, Department of Finance of Sichuan Province and Sichuan Provincial Taxation Bureau of the State Administration of Taxation
Engineering Research Center of Sichuan Province (四川省工程研究中心)	2019	Sichuan Provincial Development and Reform Commission
Chengdu New Economy Demonstration Enterprise (成都市新經濟示範企業)	2022	Chengdu New Economic Development Work Leading Group Office
Demonstration Base for Talent Recruitment (成都市引才引智示範基地)	2022	Chengdu Science and Technology Bureau (Foreign Experts Bureau)
The New Economy Gradient Cultivation Enterprises in Chengdu 2021 (2021年成都市新經濟梯度培育入庫企業)	2021	Chengdu New Economic Development and Reform Commission
2020 Rising Enterprise (2020年度雛鷹企業)	2021	Chengdu Wenjiang District New Economy and Technology Bureau

LICENSES, PERMITS AND APPROVALS

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 Advisor has advised us that, during the Track Record Period and up to 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. We are planning to renew our Use Permit for Laboratory Animals and High-tech Enterprise Certificate by their expiration date. Our PRC Legal Advisor is of the view that, there are no material foreseeable legal impediments that would prevent us from renewing such licenses, if we comply with all applicable requirements and conditions set forth in relevant laws and regulations. The table below sets forth the relevant details of the material licenses we hold for our operations in China.

License/Permit	Holder	Issuing Authority	Issue Date	Expiration Date
Drug Production License	Our Company	Sichuan Medical Products Administration	May 7, 2022	April 3, 2024
Registration Record of Class II Biosafety Laboratory of Sichuan Province for Infectable Human Pathogenic Microorganisms	Our Company	Chengdu Municipal Health Commission	December 22, 2022	December 22, 2027
Registration Record of Class II Biosafety Laboratory of Sichuan Province for Infectable Human Pathogenic Microorganism	Our Company	Chengdu Municipal Health Commission	December 22, 2022	December 22, 2027
Use Permit for Laboratory Animals	Our Company	Laboratory Animal Committee of Sichuan Province	October 24, 2018	October 24, 2023
High-tech Enterprise Certificate	Our Company	Sichuan Provincial Department of Science, Sichuan Provincial Department of Finance, Sichuan Provincial Taxation Bureau of the State Administration of Taxation	December 3, 2020	December 3, 2023

License/Permit	Holder	Issuing Authority	Issue Date	Expiration Date
Pollutant Discharge Permit	Our Company	Chengdu Ecological Environment Bureau	January 10, 2023	January 9, 2028
Consignee and Consignor of Import and Export Goods	Our Company	Chengdu Customs	April 24, 2018	N/A
Record Certificate of Explosives-Prone Hazardous Chemicals Practitioners	Our Company	Wenjiang District Branch of Chengdu Public Security Bureau	October 28, 2021	N/A
Business Registration Certificate	Our Company	Wenjiang Branch of the State Administration of Foreign Exchange	N/A	N/A

LEGAL PROCEEDING AND COMPLIANCE

During the Track Record Period and as of the Latest Practicable Date, we had not been a party to any actual or threatened material legal or administrative proceedings, and our Directors had not been involved in any such proceedings. We are committed to maintaining the highest standards of compliance with the laws and regulations applicable to our business. During the Track Record Period and up to the Latest Practicable Date, we had complied in all material respects with the applicable laws and regulations relating to our business operations. However, we may from time to time be subject to various legal or administrative claims and proceedings arising in the ordinary course of business. See "Risk Factors – Risk Relating to Our Operations – We may be involved in claims, disputes, litigation, arbitration or other legal proceedings in the ordinary course of business."

RISK MANAGEMENT AND INTERNAL CONTROL

Risk Management

We recognize that risk management is critical to the success of our business operation. Key operational risks faced by us include changes in the general market conditions and the regulatory environment of the Chinese and global biopharmaceuticals markets, our ability to develop, manufacture and commercialize our drug candidates, and our ability to compete with other biopharmaceutical companies. See "Risk Factors" for a discussion of various risks and uncertainties we face. We also face various market risks. In particular, we are exposed to credit, liquidity, interest rate and currency risks that arise in the normal course of our business. See "Financial Information – Market Risk Disclosure" for a discussion of these market risks.

We have adopted a comprehensive set of risk management policies which set out a risk management framework to identify, assess, evaluate and monitor key risks associated with our strategic objectives on an on-going basis. Risks identified by management will be analyzed on the basis of likelihood and impact, and will be properly followed up and mitigated and rectified by our Group and reported to our Directors. Our Directors supervise the implementation of our risk management policies.

To monitor the ongoing implementation of risk management policies and corporate governance measures after the [**REDACTED**], we have adopted or will continue to adopt, among other things, the following risk management measures:

- Our Directors will oversee and manage the overall risks associated with our business operations, including (i) reviewing and approving our risk management policy to ensure that it is consistent with our corporate objectives; (ii) reviewing and approving annual working plan and annual report of our corporate risk management; (iii) monitoring the most significant risks associated with our business operation and our management's handling of such risks; (iv) reviewing our corporate risk in the light of our corporate risk tolerance; and (v) monitoring and ensuring the appropriate application of our risk management framework across our Group.

- Our audit department, led by our Risk Prevention and Control Leadership Group (風險防控領導小組), will be responsible for (i) formulating our risk management policy and reviewing major risk management issues of our Company; (ii) formulating annual working plan and annual report of risk management; (iii) providing guidance on our risk management approach to the relevant departments in our Company and supervising the implementation of our risk management policy by the relevant departments; (iv) reviewing the relevant departments' reporting on key risks and providing feedbacks; and (v) education and training in relation to risk management.

- The relevant departments in our Company, including but not limited to the finance department, the legal department and the human resources department, are responsible for implementing our risk management policy and carrying out our day-to-day risk management practice. In order to formalize risk management across our Group and set a common level of transparency and risk management performance, the relevant departments will (i) gather information about the risks relating to their operation or function; (ii) conduct risk assessments, which include the identification, prioritization, measurement and categorization of all key risks that could potentially affect their objectives; (iii) continuously monitor the key risks relating to their operation or function; (iv) implement appropriate risk responses where necessary; (v) develop and maintain an appropriate mechanism to facilitate the application of our risk management framework; and (vi) timely report to our audit department and Risk Prevention and Control Leadership Group upon the discovery of material risks.

We consider that our Directors and members of our senior management possess the necessary knowledge and experience in providing good corporate governance oversight in connection with risk management and internal control.

Internal Control

Our Board is responsible for establishing our internal control system and reviewing its effectiveness. We have engaged an independent internal control consultant, or the Internal Control Consultant, to perform certain agreed-upon procedures, or the Internal Control Review, in connection with the internal control of our Company and our major operating subsidiaries and to report factual findings on our Group's entity-level controls and internal controls of various processes, including financial reporting and disclosure controls, human resources and payroll management, general controls of IT system, taxation management, contract management, and other procedures of our operations. The Internal Control Consultant performed the Internal Control Review in September and October 2022 and follow-up reviews in December 2022. As of the Latest Practicable Date, there were no material outstanding issues relating to our Group's internal control.

During the Track Record Period, we regularly reviewed and enhanced our internal control system. Below is a summary of the internal control policies, measures and procedures we have implemented or plan to implement:

- We have adopted various measures and procedures regarding each aspect of our business operation, such as related party transaction, risk management, protection of intellectual property, environmental protection and occupational health and safety. For more information, see "– Intellectual Property" and "– Social, Health, Work Safety and Environmental Matters." We provide periodic training about these measures and procedures to our employees as part of our employee training program. Our internal audit department conducts audit field work to monitor the implementation of our internal control policies, reports the weakness identified to our management and audit committee and follows up on the rectification actions.

- Our Directors (who are responsible for monitoring the corporate governance of our Group) with help from our legal advisers, will also periodically review our compliance status with all relevant laws and regulations after the [**REDACTED**]. For more details, please refer to the paragraph headed "Relationship with Our Controlling Shareholders – Corporate Governance Measures" in this document.

- We have established an audit committee which (i) makes recommendations to our Directors on the appointment and removal of external auditors; and (ii) reviews the financial statements and renders advice in respect of financial reporting as well as oversees internal control procedures of our Group.

- We have engaged First Shanghai Capital Limited as our compliance adviser to provide advice to our Directors and management team until the end of the first fiscal year after the [**REDACTED**] regarding matters relating to the Listing Rules. Our compliance adviser is expected to ensure our use of funding complies with the section headed "Future Plans and [**REDACTED**]" in this document after the [**REDACTED**], as well as to provide support and advice regarding requirements of relevant regulatory authorities in a timely fashion.

- We plan to engage a PRC law firm to advise us on and keep us abreast with PRC laws and regulations after the [**REDACTED**]. We will continue to arrange various trainings to be provided by external legal advisers from time to time when necessary and/or any appropriate accredited institution to update our Directors, senior management, and relevant employees on the latest PRC laws and regulations.

- We intend to maintain strict anti-corruption policies among our sales personnel and distributors in our future sales and marketing activities. We will also strive to ensure that our sales and marketing personnel comply with applicable promotion and advertising requirements in the future.

We will conduct periodic review of relevant laws and regulations and amend our internal policies to ensure compliance with the latest applicable laws and regulations.