OVERVIEW

We are a biopharmaceutical company committed to the discovery, development and commercialization of biologics that regulate immune microenvironment by directly modulating both the innate and adaptive immune systems. Drawing upon our expertise in immunology, we have developed various types of immunotherapies including immunocytokines to treat cancers and autoimmune diseases. We have three Core Products, IAH0968, IAP0971 and IAE0972, all of which are developed in-house. IAH0968 is an antibody-dependent cell mediated cytotoxicity ("**ADCC**") enhanced monoclonal antibody ("**mAb**"), and we have initiated Phase II clinical trials for biliary tract carcinoma ("**BTC**") and colorectal cancer ("**CRC**"). IAP0971 and IAE0972 are both immunocytokines and we have completed Phase I clinical trials for advanced solid tumors including non-small cell lung cancer ("**NSCLC**") and CRC. We stand out for our specialized focus and expertise in the development of immunocytokine products with our IAP0971 and IAE0972 among the most clinically advanced immunocytokine candidates, according to Frost & Sullivan. We aim to develop innovative immunotherapies that overcome disadvantages of currently available treatments, including low response rates and drug resistance, and to bring perceivable benefits and affordable medicine to patients worldwide.

Since our inception in 2018, we have built fully-integrated, end-to-end, in-house R&D capabilities encompassing all the key biological drug development functionalities, including discovery, antibody and protein engineering, process development, preclinical pharmacology studies, clinical development, and good manufacturing practice ("**GMP**")-compliant manufacturing. Through our proprietary technology platforms, we have identified and developed a pipeline of nine products, with six of them in clinical stage. As a leading company in exploring antibody-cytokine fusion protein based drugs according to Frost & Sullivan, we implement a global strategy for our immunocytokine products, and have obtained investigational new drug ("**IND**") approvals for conducting clinical trials of all three immunocytokines from regulatory authorities of both China and the U.S. According to Frost & Sullivan, as of the Latest Practicable Date, these three candidates were among the most clinically advanced immunocytokines in treating cancer patients in the world.

Our R&D capabilities cover development of candidates in forms of mAbs, bispecific antibodies ("**bsAbs**"), and fusion proteins, some of which extend indications into treatment areas beyond oncology. Our Core Product IAH0968 is an ADCC enhanced mAb targeting human epidermal growth factor receptor 2 ("**HER2**") with 100% fucose knock out, which greatly enhances the binding affinity of its fragment crystallizable ("**Fc**") to its receptor FcγRIIIa. Data from preclinical study showed that IAH0968 increased the binding affinity up to 20-fold comparing to trastuzumab or Herceptin, an anti-HER2 antibody without enhanced ADCC activity. The Phase I clinical data demonstrated a 40% objective response rate ("**ORR**"), and an 80% disease control rate ("**DCR**") using IAH0968 as monotherapy for heavily pretreated metastatic BTC, and CRC patients who had failed all previous therapies. Currently, we are conducting Phase II clinical trials in patients with inoperable HER2+ advanced or metastatic BTC and HER2+ metastatic CRC as first-line treatments.

Our featured products, immunocytokines, are designed through our proprietary and internally developed Armed ImmunoCytokine Platform ("**AIC^{TM} Platform**") by our core R&D team in researching antibody-cytokine fusion proteins. They function through diverse mechanisms of action yet share a similar structure comprising an antibody or quasi-antibody moiety that targets tumors and blocks signaling pathways regulating tumor growth and proliferation, and cytokine payloads that activate the immune system within the tumor microenvironment ("**TME**"). Such a design is expected to overcome drawbacks of conventional cytokine-based drugs, such as short half-lives, systemic cytotoxicity, and modest efficacies due to cytokine pleiotropy and off-target effects. It is expected to achieve enhanced antitumor effects through the synergy between the antibody and cytokine payloads, which will potentially address market demands of cancer patients who suffer from disease progression related to the immunosuppressive TME and drug resistance.

We have received IND approvals for conducting Phase I and Phase II clinical trials for our Core Products IAP0971 (PD-1/IL-15) and IAE0972 (EGFR/IL-10) in patients with advanced solid tumors from both the NMPA and the U.S. Food and Drug Administration ("**FDA**"), and completed the Phase I clinical trials in July 2023. Phase I clinical data showed that our core immunocytokine products IAP0971 and IAE0972 were well tolerated and demonstrated encouraging preliminary antitumor activities as monotherapy in heavily pretreated patients who has failed chemotherapy, targeted therapy, immunotherapy and/or their combination.

The following chart summarizes the development status of our Core Products and other selected drug candidates as of the Latest Practicable Date.

Abbreviations: 1L = first-line; 2L = second-line; 3L = third-line; ADCC = antibody-dependent cell-mediated cytotoxicity; AEA™ = ADCC Enhanced Antibody Platform; AIC™ = Armed ImmunoCytokine Platform; AIM™ = Armed Innate Effector Multispecific Platform; BCG = Bacillus Calmette-Guerin; bsAb = bispecific antibody; bsFp = bispecific fusion protein; CapeOX= capecitabine and oxaliplatin; Chemo = chemotherapy; FDA = U.S. Food and Drug Administration; GC = gemcitabine and cisplatin; IND = Investigational New Drug; mAb = monoclonal antibody; Mono = monotherapy; NMPA = National Medical Products Administration; NSCLC = non-small cell lung cancer; NMIBC = non-muscle invasive bladder cancer; BTC = biliary tract carcinoma; CRC = colorectal cancer; HBV = hepatitis B virus; HNSCC = head and neck squamous cell carcinoma; HCC = hepatocellular carcinoma; IBD = inflammatory bowel disease; Q1 = first quarter; Q2 = second quarter; Q3 = third quarter; Q4 = fourth quarter; 1H = first half; SLE = systemic lupus erythematosus.

Notes:

* All the product candidates are administered intravenously, except for IAP0971 for the treatment of 2L/3L NMIBC, which will be administered through intravesical instillation, as well as IAP0971 for the treatment of NSCLC, which will be administered through subcutaneous injection.

** We acquired exclusive rights from ImmuneOnco Biopharmaceuticals (Shanghai) Inc. to develop, manufacture and commercialize IBC0966 in Greater China including mainland China, Hong Kong, Macau, and Taiwan, as well as 7.5% of interests in the overseas rights of IBC0966. For more information, see "— Collaboration Arrangement — Collaboration Agreement With ImmuneOnco in Relation to the Development of IBC0966" in this section.

*** We have completed Phase I clinical trials of relevant products as monotherapy, and plan to leverage data collected in the respective trials and directly seek IND approvals from competent regulatory authorities to conduct Phase II clinical trials of relevant products as combination therapy.

Our pipeline includes three Core Products: one ADCC enhanced mAb, and two immunocytokines. The ADCC enhanced mAb, IAH0968, was developed based on our ADCC Enhanced Antibody Platform ("**AEA™ Platform**"). The two immunocytokines, IAP0971 and IAE0972, were developed based on our AIC™ Platform.

- **IAH0968** is a clinical stage ADCC enhanced anti-HER2 antibody with 100% removal of fucose. Binding between the Fc region and its receptor FcγRIIIa allows antibodies to activate the immune system. Studies revealed that fucose interferes with the binding between the Fc region of an antibody and FcγRIIIa. As such, complete removal of fucose can increase the binding affinity, which is expected to improve antitumor activities of antibodies. Produced through our AEA™ Platform, which is an internally developed proprietary FUT8-knock out cell line, the Fc region of IAH0968 contains 0% of fucose. Preclinical data demonstrated that IAH0968 mediated stronger ADCC killing toxicity against HER2+ tumor cells SKBR3, BT474 and SKOV2 than an anti-HER2 antibody. Moreover, IAH0968 showed 100% TGI in a BT474 tumor cell subcutaneous murine model, superior to the anti-HER2 antibody without fucose removal modification.

  The Phase I clinical trial of using IAH0968 as a monotherapy for heavily pretreated patients with advanced HER2+ malignant solid tumors including trastuzumab resistant and ineffective patients demonstrated encouraging clinical activity and tolerated safety profiles. Data showed that only one dose-limiting toxicity ("**DLT**") was found at dosage of 10mg/kg, and no maximum tolerable dose ("**MTD**") was reached. For heavily pretreated metastatic CRC and BTC patients, the ORR was 40%, and DCR was 80%. Based on these encouraging results, we have received IND approvals from the NMPA for conducting Phase II clinical trials for IAH0968 in combination with gemcitabine and cisplatin in inoperable HER2+ advanced or metastatic solid tumors and BTC on September 28, 2022, and Phase II and Phase III clinical trials for IAH0968 in combination with CapeOX in HER2+ metastatic CRC on September 28, 2022. We have completed the Phase IIa trial for CRC in March 2024, and initiated a Phase IIb/III trial for CRC in January 2024. We expect to complete the Phase IIb trial for CRC in the fourth quarter of 2024. In addition, we initiated a Phase II trial for BTC in August 2023, and expect to complete the Phase II trial in the third quarter of 2025.

- **IAP0971** is a clinical stage, dual-moiety, anti-programmed death -1 ("**PD-1**") antibody-Interleukin-15 ("**IL-15**")/its receptor ("**IL-15Rα**") heterodimer dual T cell/natural killer ("**NK**") cell agonist. It is expected to target the PD-1/its ligand ("**PD-L1**") signaling pathway to relieve the immunosuppression in the TME, and in the meantime deliver IL-15 to the tumor, and thus locally activates and enhances antitumor functions of CD8+ T cells and NK cells. Compared to marketed cytokine-based therapies, IAP0971 may offer improved safety profile through targeted delivery of IL-15, and also achieve improved efficacy profile through the *cis*-synergy between IL-15 and anti-PD-1 antibody. Furthermore, it adopts our internally designed and developed novel structure by embedding the IL-15

heterodimer in the "hinge" region of the anti-PD-1 antibody to balance the activity of IL-15 and protect IL-15 from degradation and further prolong the half-life of IAP0971. Our preclinical study showed that IAP0971 was well tolerated at a dosage up to 1.2mg/kg in the primate animal model, which is around 40-fold higher than an IL-15-Fc fusion protein. It also achieved superior tumor inhibition rate (110.47% when treated with 0.5mg/kg of IAP0971 vs. 74% when treated with 0.5mg/kg of anti-PD-1 antibody) and complete tumor regression rate (90% when treated with 0.5mg/kg of IAP0971 vs. 50% when treated with 0.5mg/kg of anti-PD-1 antibody) in our preclinical studies.

We adopted a global registration strategy for IAP0971, and has obtained IND approvals for conducting Phase I and Phase II clinical trials for advanced solid tumors from the NMPA and the FDA. Phase I study demonstrated that IAP0971 was well tolerated in heavily pretreated patients with advanced malignant tumors up to 200ug/kg Q2W when subcutaneously administered. Preliminary efficacy was observed in multiple heavily pretreated patients, including two NSCLC, who achieved stable disease ("**SD**") after receiving 120μg/kg and 200μg/kg IAP0971 monotherapy, respectively. As of the Latest Practicable Date, we have completed the Phase I study of IAP0971 and have not received objection from the NMPA for us to conduct Phase II clinical trials for IAP0971, and expect to enter Phase II clinical stage in the second quarter of 2024 in China.

- **IAE0972** is a clinical stage, dual-moiety, anti-epidermal growth factor receptor ("**EGFR**") antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation. It is designed to bind to EGFR and trigger blockage of downstream signaling pathways that contribute to cell death suppression and promote cell proliferation, and deliver IL-10 to activate CD8+ T cell in the TME. IAE0972 is designed to resolve immune cell exhaustion of current PD-1/PD-L1-based immunotherapies and lift the limitations of current EGFR-based mAbs. By specifically enriching IL-10 at EGFR-over expressing cancer, IAE0972 is expected to restore the antitumor activities of exhausted T cells. The asymmetric structure of IAE0972 employs a monovalent anti-EGFR antibody fragment to reduce its toxicity to skins. Preclinical studies showed that IAE0972 was well tolerated up to 6 mg/kg in the primate animal model, which is approximately 300 times the safe dosage of IL-10 cytokine therapy. No obvious EGFR-related skin toxicity, no significant organ changes, and no significant changes for levels of cytokines were observed. The studies showed that IAE0972 had a tumor growth inhibition ("**TGI**") rate of 83% in the mice model, which is significantly higher than an anti-EGFR antibody.

  Also following a global strategy, we have received IND approvals for conducting Phase I and Phase II clinical trials for advanced solid tumors from both the NMPA and the FDA. The clinical data from the Phase I trial indicated that IAE0972 can be safely administered to subjects at doses up to 2.5mg/kg on a weekly basis. In addition, preliminary efficacy results showed encouraging antitumor activities when IAE0972 was administered as a monotherapy in multiple heavily pretreated tumor

types including two rectal cancers. As of the Latest Practicable Date, we have concluded the Phase I study of IAE0972 and have not received objection from the NMPA for us to conduct Phase II clinical trials for IAE0972. We have initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first HNSCC patient and the first CRC patient in July 2023 and December 2023, respectively. In addition, in November 2023, we also received the IND approval from the NMPA for conducting Phase II and Phase III clinical trials of IAE0972 in combination with lenvatinib in patients with locally advanced or metastatic HCC as first-line treatment.

In addition to our Core Products mentioned above, we are developing six other product candidates: clinical stage products IBB0979, IBC0966 and IBD0333, and preclinical stage products IAN0982, ISH0988 and ISH0613.

- IBB0979, another immunocytokine developed by us based on AIC™ Platform, received IND approvals from both the FDA and the NMPA for conducting clinical trials for B7H3-high expressing solid tumors. It is an anti-B7 homolog 3 protein ("**B7H3**") antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation. It is designed to bind to B7H3 and trigger blockage of downstream signaling pathways that participate in TME shaping and development, and deliver IL-10 to activate CD8+ T cells in the TME.

- IBC0966 is a clinical stage anti-PD-L1 antibody-signal regulatory protein α ("**SIRPα**") bifunctional fusion protein. It is a therapy that stimulates both innate and adaptive immunity, leading to strong synergistic effects and long-lasting tumor-specific immune responses.

- IBD0333 also received IND approvals from both the FDA and the NMPA. It is a 4-1BB/CD24 bsAb, which simultaneously targets CD24 over expressed tumor cells and activates the stimulatory signal of 4-1BB in CD8+ T cells to induce T cell mediated antitumor immunity at the targeted tumor tissue.

- The preclinical candidates, namely IAN0982, ISH0988 and ISH0613, are currently in the IND enabling stage. IAN0982 is being developed for oncology, while ISH0988 and ISH0613 are immunosuppressors focused on autoimmune diseases.

Our commitment to innovation is evident and supported by our proprietary technology platforms, which include (1) AIC™ Platform, a scalable platform mainly concentrated on antibody-cytokine fusion protein development, (2) AEA™ Platform, a FUT8 knock-out cell line constructed to enhance the cytotoxicity of antibodies, and (3) Armed Innate Effector Multi-specific Platform ("**AIM™ Platform**"), a platform that focuses on the development of innate immunity stimulator-based bispecific/multi-specific antibodies. Each of them is designed for resolving technical difficulties and addressing drug resistance faced in developing immunotherapies and achieving optimized treatment effects. Since their launch, we have developed IAP0971, IAE0972, IBB0979, ISH0988 and ISH0613 based on AIC™ Platform, IAH0968 based on AEA™ Platform, and IAN0982 based on AIM™ Platform.

We have built our GMP-compliant manufacturing facilities, which enhance quality assurance and control of our products and fulfill clinical and potential commercial demands for our drug candidates in a cost efficient way. Our drug substance production facility is currently equipped with four production lines for a total bioreactor capacity of 1,600L. We have completed the installation of a production line for 5,000L bioreactor capacity, and completed the qualification in November 2023. Our drug product facility includes one liquid injection filing production line and one lyophilized powder production line, which enables us to prepare biological products into various dosage forms according to different needs in both clinical and commercial stages. Leveraging our GMP-compliant manufacturing capabilities, as of the Latest Practicable Date, we had successfully completed at least 30 batches with a success rate of 100%.

We are led by a management team with significant R&D experience and a proven track record. Our executive Director, chief executive officer and chief scientific officer, Dr. YIN Liusong, has over 16 years of experience in antibody and cytokine development and pipeline management, and has led more than 600 antibody drug discovery and optimization projects with dozens entered into clinical trials. Chairman of our Board and executive Director, Mr. ZHANG Feng is a pharmaceutical veteran with over 20 years of experience in the industry with expertise in R&D, clinical development, product launch and marketing. Our management team has an average of more than 15 years of industry experience in biologics development and business management, including antibody discovery and engineering, process development, GMP manufacturing, clinical operations and regulatory affairs. Their vision and insights are also key drivers of our success.

OUR STRENGTHS

Internally developed pipeline of immunocytokines with novel mechanisms of action

We are in a leading position to explore immunocytokines to modulate the TME according to Frost & Sullivan, and are experienced in overcoming technical challenges in developing them. Through insightful design of sequence, spatial structure, and protein modification, we aim to improve the safety and efficacy balancing of cytokines, which often act as a double-edge sword in modulating the immune system. Currently, our immunocytokine pipeline includes IAP0971, IAE0972 and IBB0979, all of which are drug candidates with novel mechanisms of action. All three immunocytokines have obtained IND approvals from both the FDA and the NMPA. Currently, we have concluded the Phase I study of IAP0971 and IAE0972. IAE0972 has entered the Phase II clinical phase, and IAP0971 is expected to enter the Phase II clinical phase in the second quarter of 2024. As of the Latest Practicable Date, IBB0979 was in Phase I/II clinical stage.

As potent immune mediators that play an important role in controlling the growth and activity of immune system cells, cytokines have long been deemed by researchers as a promising candidate for developing therapeutics. However, attempts to use them like conventional drugs were unsuccessful mainly due to two reasons: first, cytokines have activity on many different cell types and tissues and can cause systemic rather than localized activities; and second, cytokines are subject to biological degradation, and most of them have very short half-lives *in vivo*. As such, cytokine-based therapy with target specificity and elongated treatment window becomes a research hotspot.

We developed immunocytokines with a structure of co-expressing antibody and cytokines into a fusion protein, which is expected to overcome the drawbacks of conventional cytokine drugs and provide enhanced antitumor activities with a favorable safety profile. On one hand, the antibody portion of the fusion protein may increase the half-life and the specificity of cytokine and thus increase the treatment window and reduce the systemic toxicity. On the other hand, the cytokine portion of the fusion protein may locally activate the immune system, which will turn "cold" or immunosuppressive tumors into "hot" or immune-inflamed tumors, and thus overcome primary and acquired drug resistance.

IAP0971 – Anti-PD-1 antibody-IL-15/IL-15Rα heterodimer fusion protein

Our Core Product IAP0971 is an internally developed, dual-moiety, anti-PD-1 antibody-IL-15/IL-15Rα heterodimer dual T cell and NK cell agonist. IAP0971 is expected to synergistically strengthen the antitumor activity through blockade of the PD-1/PD-L1 signaling pathway and accumulating IL-15 at the targeted tumor site to activate its nearby immune cells, including CD8+ T cells and NK cells, directly activating both innate and adaptive immune systems. We obtained the approval for conducting Phase I and Phase II clinical trials in patients with advanced solid tumors from the NMPA and the FDA in January 2022 and December 2021, respectively.

The selection of IL-15 payload and PD-1 target was based on favorable individual features and the potential for great *cis*-synergy when combined. IL-15 can promote activation and proliferation of CD8+ T cells and NK cells, and in the meantime it does not induce regulatory T cell ("**Treg**")-related immune response suppression that is often observed for IL-2 based cytokine drugs. Also, IL-15 inhibits IL-2-induced T cell death. As such, IL-15 can stimulate CD8+ T cells and NK cells for a longer term and induce relatively fast and robust immune responses without activating Tregs or inducing apoptosis of activated T cells, which are common side effects of IL-2-based therapies.

The selection of the anti-PD-1 antibody was based on several factors, including its ability to act in the same location on the T cells and NK cells as IL-15, as well as the significantly higher expression of PD-1 on CD8+ T cells in the TME compared to peripheral blood and peripheral lymphoid organs. Therefore, the combination of IL-15 and anti-PD-1 antibody can show *cis*-synergy with lower systemic cytotoxicity. Furthermore, considering the balanced activity and dose between the PD-1 antibody and the IL-15 cytokine, IAP0971 is designed to adopt the structure of an intact bivalent anti-PD-1 antibody in combination with a monovalent IL-15. As such, the combination can deliver targeted and controlled amount of IL-15 directly into the TME, which effectively recruits, activates, and reinvigorates immune cells, leading to a significantly enhanced antitumor immunity.

Structure of IAP0971 is also optimized to improve biological activities, developability and productivities. The cytokine moiety of IAP0971 is designed to adopt a structure of IL-15 combining with its receptor IL-15Rα to form a heterodimer that resembles its natural state. On the one hand, the natural high affinity between IL-15 and IL-15Rα avoids the formation of IL-15 homodimer and half antibody fragment, and reduces the mismatch of two different heavy

chains of the anti-PD-1 antibody, which improves the productivity of IAP0971. On the other hand, the IL-15/IL-15Rα complex adopted in IAP0971 is reported to be more active than IL-15 alone in stimulating proliferation and survival of memory phenotype CD8+ T cells. In addition, the spatial structure of IAP0971 is also optimized by embedding the IL-15/IL-15Rα heterodimer in the "hinge" region of the anti-PD-1 antibody. This structure can balance the dose of IL-15 cytokine with that of the PD-1 antibody, as well as prevent degradation of IL-15, thereby prolonging the half-life of IL-15.

Preclinical data showed that IAP0971 was well tolerated up to 1.0mg/kg when subcutaneously administered in MC38 syngeneic mouse model. In the repeated-dose toxicity study in cynomolgus monkeys, IAP0971 showed a favorable safety profile even at 1.2mg/kg, around 40-fold higher than an IL-15-Fc fusion protein. Furthermore, in pharmacokinetic analysis, IAP0971 showed a half-life of 15.7 hours, which is approximately 15-fold longer than that of recombinant IL-15, and approximately 2-fold longer than that of an IL-15-Fc fusion protein. In addition, IAP0971 achieved superior tumor inhibition rate (110.47% when treated with 0.5mg/kg of IAP0971 vs. 74% when treated with 0.5mg/kg of anti-PD-1 antibody) and complete tumor regression rate (90% when treated with 0.5mg/kg of IAP0971 vs. 50% when treated with 0.5mg/kg of anti-PD-1 antibody) in our preclinical study.

In July 2023, we have completed the Phase I clinical trial of IAP0971 for advanced malignant tumors. Data showed that IAP0971 exhibited a favorable safety profile at up to 200μg/kg in patients with advanced solid tumors, with no DLT and MTD observed. Preliminary antitumor efficacy was observed in four patients treated with IAP0971 as a later-line therapy. These four patients include one with CRC, one with cervical cancer, and two with NSCLC, and these patients underwent multiple rounds of treatments including chemotherapy, targeted therapy, immunotherapy and/or their combination, and experienced disease progress and metastasis. After receiving IAP0971 for two treatment cycles, all four patients achieved stable disease ("**SD**"). Especially, one NSCLC patient complicated with adrenal gland and other metastases was resistant to several prior treatments, including chemotherapy regimes such as multiple paclitaxel-containing combination, and combination therapies with targeted therapy and immunotherapy, such as erlotinib, camrelizumab, sintilizumab and bevacizumab. This patient received 120μg/kg IAP0971 for two treatment cycles and achieved SD. The other NSCLC patient complicated with pleura or pleural effusion metastases who was resistant to several prior treatments, also achieved SD after two cycles of 200μg/kg IAP0971 administration. Based on the encouraging Phase I results and without objection from the NMPA, we expect to commence a Phase II clinical trial for IAP0971 in China in the second quarter of 2024.

IAE0972 – Anti-EGFR antibody-IL-10 homodimer bifunctional fusion protein

Our Core Product IAE0972 is an internally developed, dual-moiety, anti-EGFR antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation. Like IAP0971, IAE0972 is also expected to achieve synergistical antitumor activities leveraging the advantages of immunocytokine yet through a different combination of antibody target and cytokine payload. It is designed to blockade the EGFR signaling pathway and specifically

deliver IL-10 to the targeted tumor site to activate CD8+ T cells, and potentially NK cells. We obtained the approval for conducting Phase I and Phase II clinical trials in patients with advanced solid tumors from the FDA and the NMPA in December 2021 and January 2022, respectively.

The development of IAE0972 aimed to address the issue of immune cell exhaustion observed in current PD-1/PD-L1-based immunotherapies and overcome the limitations of current EGFR-based mAbs. IL-10 is a potent activator of tumor-infiltrating memory cytotoxic antigen-specific CD8+ T cells in the TME and can restore the tumor-killing activity of tumor-infiltrating terminally exhausted T cells. Because the anti-EGFR antibody fragment can specifically enrich IL-10 in the TME, IAE0972 can effectively and specifically activate the immune system by reinvigorating antigen specific CD8+ T cells and facilitating its proliferation, and inhibiting tumor growth by blocking the EGFR signaling pathway to kill EGFR-positive tumor cells. As a result, it is expected to resolve the issues of low ORR and drug resistance commonly observed with anti-EGFR antibodies.

Like IAP0971, IAE0972 also adopts the natural structure of IL-10, which is in a homodimer form, so that the natural pairing between IL-10 molecules will improve the developability and productivity of IAE0972. But unlike IAP0971, IAE0972 adopts an asymmetric structure, which consists of a monovalent anti-EGFR antibody fragment and a homodimer of IL-10. Such a design is expected to reduce the binding activity of anti-EGFR antibody on EGFR-low expression normal cells while preserving the biological activity on EGFR-high expression tumor cells and thus reduce EGFR-related skin toxicities. In addition, the spatial structure of IAE0972 employs the knobs-into-holes format in the Fc to promote asymmetric formation and improve its developability. This optimization extends the half-life of IL-10 and improves its therapeutic efficacy.

In vivo data of the preclinical study showed that IAE0972 was well tolerated up to 6 mg/kg in cynomolgus monkeys, which is 300 times the safe dosage of IL-10 cytokine therapy. Also, no obvious EGFR-related skin toxicity, no significant organ changes for liver, thymus, adrenal gland and thyroid gland, and no significant changes for levels of IL-2, tumor necrosis factor-alpha ("**TNFα**") and Interferon-gamma ("**IFNγ**") were observed in the cynomolgus monkey repeated-dose toxicity studies. Studies showed that IAE0972 had a TGI rate of 83% in a MC38-hEGFR syngeneic mice model, which rate is significantly higher than that of an anti-EGFR antibody.

In our Phase I clinical trial of IAE0972 for advanced solid tumors, we recruited 14 patients with advanced esophageal squamous cell carcinoma, rectal cancer, gastric cancer, pancreatic cancer, SCLC or NSCLC who progressed from at least one line of treatment. We have completed dose escalation for 1μg/kg, 10μg/kg, 100μg/kg, 0.3mg/kg, 1.0mg/kg and 2.5mg/kg of IAE0972, and have only observed one Grade 3 adverse events. No DLT occurred and MTD was not reached. As of the Latest Practicable Date, preliminary efficacy was observed in multiple heavily pretreated patients who failed all previous therapies. A CRC patient complicated by lung metastasis, who has received multiple lines of prior treatments including standard mFOLFOX6 (5-fluorouracil, leucovorin and oxaliplatin) and CapeOX

(capecitabine and oxaliplatin) regimens, achieved SD after given 10μg/kg of IAE0972 for two treatment cycles. Another patient with rectal cancer and lung metastasis and lymph mode metastasis, who had experienced recurrence after two resections, achieved SD after receiving 1.0mg/kg of IAE0972 monotherapy for two cycles. The Phase I clinical trial was completed in July 2023. Based on the encouraging Phase I results and without objection from the NMPA, we have initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first HNSCC patient and the first CRC patient in July 2023 and December 2023, respectively.

IBB0979 – an anti-B7 homolog 3 protein ("B7H3") antibody-IL-10 homodimer bifunctional fusion protein

IBB0979, another immunocytokine developed by us, is a clinical stage anti-B7H3 antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation. It is designed to bind B7H3 and trigger blockage of downstream signaling pathways that participate in TME shaping and development, and deliver IL-10 to activate CD8+ T cells to fight against tumors. Preclinical study showed that IBB0979 has high affinity to both targets and exhibited potent TGI in C57BL/6J mice bearing MC38-hB7H3 cell line, with TGI of 100% at 0.3mg/kg, 1mg/kg and 3mg/kg. An *in vivo* study in cynomolgus monkeys showed that after intravenously administered with 1mg/kg, 2mg/kg and 6mg/kg of IBB0979 once a week for 29 days (5 times in total, given in days 1, 8, 15, 22 and 29), MTD was not reached up to 6 mg/kg. There was no administration-related mortality, and no donor-related changes observed.

We obtained the approval for conducting Phase I and Phase II clinical trials in patients with advanced solid tumors from the FDA and the NMPA in October 2022 and November 2022, respectively. The Phase I clinical trial is currently on-going, with the first patient dosed in July 2023. Since B7H3 is overexpressed in a wide range of cancers including glioma, thyroid, lung, head and neck, rectal, prostate, breast, skin, renal cell, and ovarian cancers, it has the potential to become a next-generation therapy for alleviating T cell exhaustion in cancer patients.

Differentiated products developed leveraging our insights on immunology and antibody engineering

In addition to our immunocytokine pipeline, we leverage our insights on immunology and our significant expertise in biologics design and antibody engineering to develop immunotherapies, which exert antitumor activities through novel mechanisms of action. These candidates are designed to achieve improved outcome comparing to currently approved drugs. IAH0968 and IBD0333 exemplify our drug design roadmap based on our understanding of immunological mechanisms of action and spatial structures of biologics, and our engineering capabilities in accomplishing the conception.

IAH0968

Our Core Product IAH0968 is an internally developed, the first anti-HER2 antibody in clinical stage with 100% fucose-removal. It is designed with an aim to achieve enhanced ADCC activities compared to current anti-HER2 antibodies. While no head-to-head study was conducted, the Phase I clinical data showed that IAH0968 achieved significantly improved ORR and DCR in heavily pretreated metastatic CRC and BTC patients, when compared to the historical data of current treatments. We obtained an IND approval from the NMPA for conducting Phase II clinical trials for IAH0968 in combination with gemcitabine and cisplatin in HER2+ patients with inoperable advanced or metastatic tumors and BTC, and another IND approval from the NMPA for conducting Phase II and Phase III clinical trials for IAH0968 in combination with CapeOX in HER2+ patients with metastatic CRC.

Antibodies consist of two structural regions, antigen binding fragment ("**Fab**") and Fc. Unlike Fab region, which defines the specific target of an antibody, Fc region mediates ADCC by activating the immune system through engaging various Fc receptors. Different approaches have been adopted to achieve enhanced ADCC, mainly including Fc point specific mutation, such as through amino acid alterations (e.g. margetuximab and inetetamab) and fucose removal. Fucose removal can be achieved either through the post-expression modification by enzyme digestion or through the construction of new cell lines. Studies of the structure of the Fc region of antibodies and its receptor FcγRIIIa complex revealed that the core fucose of the Fc region is accommodated at a place that interferes with the binding between the Fc region and FcγRIIIa, and thus reducing the affinity between them and resulting in lower ADCC activity. Therefore, modifying to remove fucose is desirable to better recruit immune cells, resulting in enhanced ADCC activity. As a result, this approach has been widely attempted in the biopharmaceutical industry. However, despite numerous attempts by multiple players to modify antibodies through various approaches, most resulting antibodies still contain a certain percentage of core fucose.

We addressed this technical difficulty through constructing a new cell line with mutated FUT8, which encodes an enzyme that catalyzes the transfer of fucose residue from its donor to its target. After biological engineering, the new cell line is not able to attach fucose to any protein it produced. In such a way, we have successfully generated potentially the first anti-HER2 antibody with 100% removal of fucose from its Fc region, i.e. IAH0968. Such achievement has been verified through glycoprotein detection and glycosylation quantification.

Produced through our AEA™ Platform, IAH0968 showed an affinity between IAH0968 and its Fc receptor ten to 20 times higher than unmodified or other ADCC enhanced anti-HER2 antibodies in preclinical studies (especially for the FcγRIIIa 158F polymorphism). *In vitro* assays demonstrated that IAH0968 mediated stronger ADCC killing toxicity against HER2+ tumor cells SKBR3, BT474 and SKOV2 than trastuzumab. Moreover, IAH0968 showed 100% TGI in a BT474 tumor cell subcutaneous murine model, superior to trastuzumab, an anti-HER2 antibody that does not go through fucose removal. In cynomolgus monkeys, IAH0968 showed an encouraging safety profile, with no observed adverse effect at a dosage over 100mg/kg.

The Phase I clinical trial showed that IAH0968 was well tolerated and exhibited antitumor activities in patients with advanced HER2+ malignant solid tumors including breast cancers, gastric cancers, CRC and BTC with drug resistance to trastuzumab, pertuzumab, cetuximab, docetaxel, oxaliplatin, capecitabine, irinotecan, nab-paclitaxel and apatinib, or anti-PD-1 mAbs. Data showed that only one DLT was found at dosage 10mg/kg and no MTD was reached. For heavily pretreated metastatic CRC and BTC patients, the ORR was 40%, and DCR was 80%. As of September 28, 2022, we had obtained IND approvals from the NMPA to conduct Phase II and Phase III clinical trials of using IAH0968 in combination with chemotherapy for first-line treatment of HER2+ advanced or metastatic CRC and BTC patients. We have dosed the first patient in May 2023 in a Phase II trial to evaluate IAH0968 in combination with chemotherapy in HER2+ metastatic CRC, completed the Phase IIa trial in March 2024, and entered a Phase IIb/III trial in January 2024. In August 2023, we have also dosed the first patient in a Phase II trial to evaluate IAH0968 in combination with gemcitabine and cisplatin in inoperable HER2+ advanced or metastatic BTC. We expect to complete the Phase IIb clinical trial for CRC in the fourth quarter of 2024, and complete the Phase II clinical trial for BTC in the third quarter of 2025.

IBD0333

IBD0333 is an internally developed, clinical stage, 4-1BB/CD24 bsAb, which simultaneously targets CD24 over expressed tumor cells and activates the stimulatory signal of 4-1BB in CD8+ T cells to induce T cell mediated antitumor immunity at the targeted tumor tissue. Developed from our proprietary bispecific antibody platform, IBD0333 exemplifies our research capabilities in designing and developing bispecific antibodies.

IBD0333 is potentially the first bsAb that targets both 4-1BB and CD24. CD24 is highly expressed in many cancers, such as ovarian and breast cancer and its high expression is often related to poor prognosis. CD24, expressed on the surface of tumor cells, and sialic-acid-binding Ig-like lectin 10 ("**Siglec-10**"), expressed on immune cells, act as an innate immune checkpoint that is essential for mediating antitumor immunity. The interaction between them promotes tumor immune escape. By specifically targeting CD24, IBD0333 will not only be able to target cancer cells that overexpress CD24, but also block the CD24/Siglec-10 interaction to prevent immune escape. 4-1BB is a costimulatory molecule expressed on immune cells including CD8+ T cells and also DC cells, monocytes, B cells, mast cells, NK cells and neutrophils. 4-1BB's activation triggers a signaling cascade that activate both innate and adaptive immune system, resulting in upregulation of antiapoptotic molecules, cytokine secretion, and enhanced effector function. Because anti-4-1BB antibody was known to have hepatotoxicity, tumor-associated antigens ("**TAA**") targeting to specifically activate immune cells in the TME is expected to enhance its safety profile.

In addition to the target selection, IBD0333 has additional structural design aiming to achieve improved safety and efficacy. For example, the anti-4-1BB moiety is designed to activate the 4-1BB signaling pathway only when IBD0333 binds to the tumor cells that overexpress CD24, which can further reduce the systemic toxicity of the product. The antibody backbone of IBD0333 is an IgG4, which binds to its receptors with lower affinity (except for

FcRI), and is a poor inducer of Fc-mediated effector functions. By adopting IgG4 as its backbone antibody, IBD0333 can further reduce the safety risk of anti-4-1BB antibody. Through targeted delivery of anti-4-1BB moiety and specific activation of the stimulatory signal of immune cells in the TME, IBD0333 can achieve not only improved safety, but also improved efficacy compared to anti-4-1BB mAbs.

Preclinical data showed that IBD0333 had excellent safety and efficacy profile. In toxicology studies of IBD0333 in both mice and cynomolgus monkeys, no obvious abnormality in mice or cynomolgus monkeys administered with IBD0333 was observed. The MTD was estimated to be greater than 200mg/kg with no severe side effects observed in the study. Benchmark anti-4-1BB mAbs, Utomilumab from Pfizer and Urelumab from BMS, were reported to show either systemic toxicity or hepatotoxicity at 30mg/kg and 0.3mg/kg in the Phase III trials, respectively. Comparing to these mAbs, the 200mg/kg MTD of IBD0333 according to the preclinical data showed that IBD0333 has great potential to achieve significantly improved safety profile. As to efficacy, IBD0333 showed excellent tumor inhibition activities in mice model with 99% tumor growth inhibition at 1mg/kg and 100% at 3mg/kg, in a dose-dependent manner. We have obtained IND approvals from the FDA on June 2, 2023 and from the NMPA on July 10, 2023, dosed the first patient of a Phase I clinical trial in March 2024, and plan to complete the Phase I trial in the third quarter of 2025.

Proprietary platforms aimed to addressing bottlenecks of current immunotherapies continue fueling the development of differentiated biological products

Our R&D capabilities are driven by our proprietary platforms, including AIC™ Platform, AEA™ Platform, and AIM™ Platform. We built our pipeline mostly based on them with our in-depth understanding of immune microenvironment.

AIC™ Platform

Our AIC™ Platform is prominently positioned in the field of immunocytokine development from multiple aspects, including cytokine selection and optimization, antibody selection and engineering, structural design and engineering, and production through customized cell line. It is a comprehensive research engine that includes not only a pool of intact immunoglobulin G ("**IgG**") antibodies and cytokines, but also functional antibody fragments and other types of immune system modulators. It is able to generate products ranging from immunocytokines to other bifunctional fusion proteins. Our clinical stage drug candidates IAP0971, IAE0972 and IBB0979, and preclinical stage drug candidate ISH0988 and ISH0613 were developed based on the AIC™ Platform.

Our AIC™ Platform successfully addresses technical difficulties for developing immunocytokines. These difficulties range from antibody and cytokine selection and optimization, to final drug production.

- Antibody/cytokine selection. Due to different spatial structure, different types of cytokines behave largely different when fused with antibodies targeting different antigens.

- Structural design. Dose ratio and activity between the selected antibody and cytokine is needed to be balanced to achieve the desired mechanism of actions ("**MoA**") and synergistic effects.

- Manufacturing capabilities. It is challenging for developing and manufacturing immunocytokine molecules, because they are structurally complicated, especially considering the degradation vulnerability of cytokines.

Core competencies of AIC™ Platform include MoA-based antibody-cytokine selection, biology-oriented structural design and protein engineering, and production through customized cell line.

- MoA-based antibody-cytokine selection is the cornerstone to achieve desired synergistic effects between antibody and cytokine. For example, selection of anti-PD-1 antibody and IL-15 cytokine for developing IAP0971 is grounded on their shared action site on the same T/NK cells, leading to great *cis*-synergy. The combination of anti-EGFR antibody and IL-10 is selected based on the potential engager effects it can produce. Specifically, IAE0972 can engage CD8+ T cells through IL-10 while simultaneously targeting tumor cells through the EGFR antibody moiety.

- Structural design and protein engineering module enable us to structurally design and modify our products to achieve improved safety and efficacy profile while reducing manufacturing cost and enhancing product quality manageability. Structural modifications that we are capable to perform through AIC™ Platform include antibody and cytokine engineering, deglycosylation, linker/spacer design and optimization, and tertiary structure alteration. Especially, developed through the AIC™ Platform, IAP0971 employs the natural pairing of IL-15/IL-15Rα, which leads to more efficient dimerization and eliminates the formation of IL-15 homodimer and half antibody fragments. Additionally, a knobs-into-holes structure is introduced in the Fc region of the anti-PD-1 antibody, reducing the mismatch of two different heavy chains. These structural designs result in improved productivity of IAP0971. Furthermore, IAP0971 is also modified by engineering the IL-15/IL-15Rα heterodimers partially embedded into the "hinge" region in the anti-PD-1 antibody. Our drug candidate is the first of this structure to enter into clinical trial, according to Frost & Sullivan. It can increase the stability of cytokine by "hiding" a substantial portion of cytokine within antibody to protect it from hydrolysis by proteases, as well as balances the activity of cytokine versus antibody by introducing steric hindrance to the cytokine, and in the meantime retains the specificity and affinity of cytokine to bind to its receptor and allows it to mediate immune responses.

- Production through customized cell lines is another important function performed by our AIC™ Platform. The cell lines we constructed for producing immunocytokines and other bifunctional fusion proteins are obtained after undergoing multiple rounds of metabolic and growth optimization and are of high expression capacity and excellent purification yield. Coupled with unique cytokine-specific codon optimization, stably expressed vehicles with optimized expression cassettes and our high-throughput screening system, it is able to reach an expression level of 4g/L and one-step affinity chromatography purity of 86%, which is at the top level among rivals both at home and abroad, according to Frost & Sullivan.

AEA™ Platform

Our AEA™ Platform is a biologically engineered Chinese hamster ovary ("**CHO**") cell line with the FUT8 knocked-out to generate antibodies with enhanced ADCC and improved antitumor activities. Through this bioengineering modification, the CHO cell line will not be able to catalyze the transfer of fucose residue from its donor to its target, and thus is not able to produce any antibody that carries fucose. Because absence of core fucose on the Fc region has been shown to increase the Fc region's binding affinity (up to 100 times) to its receptor FcγRIIIa present on immune effector cells, fucose-negative antibodies are expected to have enhanced ADCC activities through better activating immune effector cells.

Comparing to other platforms that aim to achieve enhanced ADCC by removing fucose from antibodies, AEA™ Platform is expected to produce antibodies with 0% of fucose, which rapidly, stably, and thoroughly enhances the ADCC of antibodies and simplifies quality control of the products. Different biological engineering has been adopted by different platforms. However, seldom platforms achieved 100% fucose removal. As of the Latest Practicable Date, our AEA™ Platform and POTELLIGENT from Kyowa Kirin are the only two platforms that can achieve 100% fucose removal rate, according to Frost & Sullivan.

Feasibility and advantages of AEA™ Platform have been demonstrated by IAH0968, the first complete fucose-removal anti-HER2-antibody in clinical stage developed through this platform. We have verified through glycoprotein detection and glycosylation quantification that IAH0968 does not contain any fucose. In addition, *in vitro* and *in vivo* tests showed that the affinity between IAH0968 and its Fc receptor was ten to 20 times higher than unmodified or other ADCC enhanced anti-HER2 antibodies, resulting in greater enhanced ADCC activity and antitumor efficacy.

AIM™ Platform

Our AIM™ Platform focuses on designing multi-functional biological products by engaging the innate immune system for cancer immunotherapy. It selects tumor associated antigen antibodies for cancer targeting, receptors agonist antibodies for innate effector activation, and cytokines and other TME factors for immune modulation to design multi-specific antibody fusion proteins, and evaluates them in terms of expression, target binding, *in vitro* and *in vivo* biological activities, as well as druggability. Currently, we have developed

several categories of our proprietary AIM™ Platform that allow us to explore the combination of innate immunity stimulators with different types and numbers of targets, which provide us with abundant flexibility and diversity of various types of TME modulations for different clinical indications.

By targeting innate immunity stimulators instead of adaptive immunity stimulators, which is considered more cytotoxic and easily restrained by immune escape of tumors and the immunosuppressive TME, products developed from our AIM™ Platform are expected to achieve desired clinical safety and efficacy profiles. Our preclinical product IAN0982 was developed based on the AIM™ Platform.

Fully integrated, end-to-end, in-house drug development capabilities encompassing all key biologic drug development functionalities

We have built and continue to build key capabilities and infrastructure that empower us to advance a broad portfolio of programs to the clinic. Within five years since our inception, we have established fully integrated, end-to-end, in house drug development capabilities covering functions of drug discovery and preclinical studies, process development, GMP-compliant manufacturing, clinical development, and quality control. Leverage these capabilities and through efficient execution of our R&D strategies, we have developed multiple proprietary technology platforms, from which we have generated a pipeline of nine product candidates, with six of them in the clinical stage.

Our achievement is largely attributed to our R&D team, who has profound industry experience in fields such as mechanisms of cytokine action, antibody drug discovery, protein engineering and antibody engineering, and biopharmaceutical project management. Our core R&D team members are experienced project leaders in the pharmaceutical industry. They contributed their knowledge and provided guidance to the development of our proprietary R&D platforms and drug candidates. As of the Latest Practicable Date, we have a dedicated in-house R&D team with 57.5% of team members holding masters or doctorate degrees in biology or medical related majors.

Our clinical development and regulatory affairs handling capabilities cover China and the U.S., which empower us to adopt a global strategy for the development of our product candidates. As of the Latest Practicable Date, except for IBC0966, we held global commercial rights of all of our pipeline products. Our clinical development team manages our clinical trials and carries out substantial clinical development activities, including clinical trial design, implementation, the collection and preliminary analysis of trial data, and communication with regulatory authorities. As of the Latest Practicable Date, we have successfully secured five IND approvals from the FDA by leveraging our clinical execution capabilities and through our regulatory affairs team members' broad and close communication with clinical development specialists in FDA regulations.

Our chemistry, manufacturing and controls ("**CMC**") team is experienced in GMP-compliant manufacturing. We have established our own manufacturing facilities in Nanjing, PRC in compliant with international GMP standards regulated by the NMPA, FDA and European Medicines Agency ("**EMA**"), which meet both clinical and commercial production demands of our drug candidates. Our four drug substance production lines for a total bioreactor capacity of 1,600L are currently in operation, and have successfully completed over 30 production batches of immunocytokines, mAbs, bsAbs and fusion proteins, which fulfilled the needs for performing preclinical study, pilot production of antibody drugs and conducting early phase clinical trials. We have completed the installation of a production line for 5,000L bioreactor capacity, and completed the qualification in November 2023. When putting into operation, it will enable us to manufacture our drug candidates for Phase III clinical trials and commercialization in-house. Our drug production facility includes one commercial-scale liquid injection filing production line and one commercial scale lyophilized powder production line, which enables us to prepare biological products into various dosage forms according to different needs.

Experienced management team of industry veterans with a proven record of success

We have assembled an experienced management team of successful industry veterans, who have an average of more than ten years of experience in drug development or manufacturing, or business management in well-reputed biopharmaceutical companies in China or abroad, and led the discovery, development and marketing of multiple target therapies, biologics and biosimilars.

Dr. Yin, our executive Director, chief executive officer, and chief scientific officer, has 16 years of experience in immunology and biologics development with eight years in leadership roles. He has led more than 600 of antibody drug discovery and optimization projects, many of which entered into clinical stage. He was named as an inventor of more than 70 patents directed to innovative biologics, and more than 10 projects were out-licensed to reputable biotechnology companies. As of the Latest Practicable Date, Dr. Yin has published 16 research papers in journals indexed in Science Citation Index ("**SCI**"), and these papers were cited by others for more than 500 times. In addition to his role as an industry leader, he serves as an adjunct professor at Institute of Microbiology of Chinese Academy of Sciences. Dr. Yin received his Bachelor of Science in biological sciences from University of Science and Technology of China, and Doctor of Philosophy in Biomedical Sciences in University of Massachusetts Chan Medical School in the U.S.

Chairman of our board and executive director, Mr. Zhang is experienced in R&D, clinical development, product launch, and marketing. He is a serial entrepreneur and veteran pharmaceutical professional with over 20 years of experience in the industry. Besides, Mr. Zhang has successfully obtained marketing approvals for nearly 20 drugs, manufacturing certificates for over 30 drugs, and has involved in the development of more than 50 clinical and preclinical products, 15 of which are Class 1 or Class 2 new drugs according to the drug classification standards issued by the NMPA. In addition to his leadership in the pharmaceutical industry, Mr. Zhang holds multiple positions in academia and industry

organizations. Particularly, he is a member of the sixth editorial board of Progress in Pharmaceutical Sciences 《藥學進展》, a committee member of the Antitumor Drug Committee of the Chinese Pharmaceutical Association (中國藥學會抗腫瘤藥物專業委員會), and the vice president of the Jiangsu Provincial Pharmacy Association (江蘇省醫藥行業協會).

Members of our senior management team are pragmatic and experienced industry leaders with a proven record of success in drug development. The head of R&D department, Ms. JIANG Xiaoling, has over 15 years' experience in R&D of pharmaceuticals including biosimilar drugs and antibody drugs. She led the development of about 20 innovative biologics and six biosimilars. Mr. JIANG Dongcheng, the leader of our manufacturing team, who has 10 years' experience in GMP manufacturing, has directly involved in GMP-manufacturing, scaling-up, validation of more than ten drug candidates.

OUR STRATEGIES

We aspire to be a leading global biopharmaceutical company with a focus on antibody and cytokine-based therapeutics. Our mission is to bring perceivable benefits and affordable medicine to patients both in China and globally. We intend to execute the following strategies to achieve our aspiration and mission.

Focus on the development of immunocytokines to enhance our position in this drug development field

We plan to fully explore our knowledge and experience in developing immunocytokines and rapidly advance the clinical development of our immunocytokine product candidates, including IAP0971, IAE0972 and IBB0979. We will also continue developing and further exploring our AIC™ Platform to enrich our immunocytokine pipeline.

Rapidly advance clinical development of immunocytokines

- **IAP0971**. We completed the Phase I clinical trial of IAP0971 administered subcutaneously for advanced malignant tumors in July 2023, and plan to initiate the Phase II clinical trials in 2L advanced NSCLC patients in the second quarter of 2024. In addition, we received the IND approvals for conducting Phase I and Phase II clinical trials for IAP0971 administered intravesically in patients with recurrent or metastatic non-muscle invasive bladder cancer ("**NMIBC**") from NMPA and the FDA in May 2023 and August 2023, respectively. We expect to complete the Phase I study and enter a pivotal Phase II trial in the fourth quarter of 2024. Furthermore, PD-1 or PD-L1 is significantly upregulated in the liver of chronic hepatitis B patients, skewing the immune response towards the induction of tolerance in circulating naïve T cells and attenuating the effector functions of liver-infiltrating cytotoxic T lymphocytes. To fully explore IAP0971's clinical potential, we also plan to submit the IND for conducting clinical trials of IAP0971 for the treatment of chronic HBV infections in the third quarter of 2024.

- **IAE0972**. We have completed the Phase I clinical trial of IAE0972 for locally-advanced or metastatic solid tumors in July 2023, initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first HNSCC patient and the first CRC patient in July 2023 and December 2023, respectively. In addition, we received the IND approval from the NMPA for conducting Phase II and Phase III clinical trials of IAE0972 in combination with lenvatinib in patients with locally advanced or metastatic HCC as first-line treatment in November 2023. We expect to commence a Phase II clinical trial for HCC in the second quarter of 2024. Furthermore, we also plan to submit an IND application for and initiate a Phase II clinical trial of IAE0972 in combination with docetaxel for NSCLC in the third quarter of 2024.

- **IBB0979**. We are currently conducting a Phase I clinical trial of IBB0979 for locally-advanced or metastatic solid tumors with IND approved by both the FDA and the NMPA. We expect to complete the Phase I clinical trial, and enter Phase II clinical stage for extensive-stage small cell lung cancer ("**ES-SCLC**") and metastatic castration-resistant prostate cancer ("**mCRPC**") in the fourth quarter of 2024.

Continue developing AIC™ Platform and enriching our pipeline therefrom

We will continue scaling-up our AIC™ Platform to design and develop new molecules with innovative mechanism and novel targets, and expand indications of our immunocytokines beyond oncology. Leveraging technical advantages of our AIC™ Platform, in addition to immunocytokines, we intend to develop and are also capable of developing products containing functional groups that have a similar function of regulating inflammation signaling pathways as cytokines. IBC0966, an anti-PD-L1 antibody-SIRPα fusion protein, marks our first attempt in developing an antibody fusion protein that carries immune system modulators that play a similar role as cytokines. We have conducted preclinical studies of IBC0966 since its acquisition, completed the Phase I trial of IBC0966, and expect to enter into Phase II clinical stage in the second quarter of 2024.

In addition, our AIC™ Platform also enables us to design product candidates that suppress immune responses. Currently, our immunocytokine pipeline products are potent immunostimulants that directly activate both innate and adaptive immunity. Our AIC™ Platform is scalable to develop immunoregulators including immunosuppressors, which enables us to enrich our pipeline with candidates for the treatment of autoimmune diseases and emergency care against cytokine storm. We have developed ISH0988, an anti-inflammatory and tissue-protective bifunctional fusion protein that is currently in preclinical study phase for the treatment of inflammatory bowel disease ("**IBD**"), and ISH0613, a bifunctional antibody fusion protein that simultaneously inhibits B cell activation and IFNα secretion for the treatment of systemic lupus erythematosus ("**SLE**"), based on the AIC™ Platform. In the future, leveraging the AIC™ Platform, we plan to develop immunocytokines or other types of fusion proteins targeting pro-inflammatory signaling pathways that are associated with autoimmune diseases.

Explore new immunocytokine development platforms

In addition to continue developing our AIC™ Platform, we plan to develop a novel immunocytokine prodrug platform, which will allow us to design prodrugs that is pharmacologically inactive, and is metabolized into an active drug after it enters the human body. This platform is expected to deliver products with improved safety, prolonged therapeutic window, and more balanced profile between efficacy and safety, and thus will further enhance our current position in the immunocytokine development field.

Continue advancing selected pipeline products with great clinical value and commercial potential

In addition to our featured immunocytokines product candidates, we intend to continue advancing selected products and expanding indication coverage.

Continue advancing selected pipeline products

- **IAH0968**. We are currently conducting a Phase II clinical trial for IAH0968 in combination with CapeOX in HER2+ metastatic CRC and a Phase II clinical trial for IAH0968 in combination with gemcitabine and cisplatin in inoperable HER2+ advanced or metastatic BTC. We have completed the Phase IIa clinical trial for CRC in March 2024, commenced a Phase IIb/III clinical trial for CRC in January 2024, and plan to complete the Phase IIb trial in the fourth quarter of 2024. We also plan to submit a BLA of IAH0968 for the treatment of 1L HER2+ advanced BTC to the NMPA in the second half of 2025.

- **IBD0333**. We have received the IND approvals for conducting clinical trials of IBD0333 for locally-advanced or metastatic solid tumors from both the NMPA and the FDA in July 2023 and June 2023, respectively. We initiated a Phase I clinical trial in March 2024 in patients with locally advanced/metastatic solid tumors. We expect to complete the Phase I study in the third quarter of 2025.

- **IBC0966**. We obtained the IND approval from the NMPA for conducting Phase I and Phase II clinical trials of IBC0966 in advanced malignant tumors in March 2021. We concluded the Phase I study in December 2023, and expect to enter Phase II clinical trials for non-Hodgkin lymphomas ("**NHL**") in the second quarter of 2024.

Continue to advance and enrich our product pipeline in autoimmune diseases and viral infections

Leveraging our strong in-house R&D capabilities, we have developed two product candidates, i.e. ISH0988 and ISH0613, indicated for autoimmune diseases IBD and SLE. ISH0988 can inhibit either upstream B cell activation by anti-self antibodies or downstream INFα production by immune cells and deliver precise immunotherapy to treat the disease, while ISH0613 can achieve anti-inflammatory and tissue-protective functions. We will continue advancing these preclinical products into clinical stage, and expect to submit IND applications to both the NMPA and the FDA in the second quarter of 2024.

We will continue to discover and generate lead candidates to enrich our early-stage pipeline. These include innovative drug candidates against novel or validated targets for autoimmune diseases. We plan to continue to design and develop bifunctional biologics to modulate immune responses, like ISH0988 and ISH0613, and optimize these biologics to enhance their efficacy, safety and pharmacokinetic properties. This involves sequence optimization, spatial structural modification, and adjusting binding affinities to different targets.

We will continue developing treatments for viral infections through two approaches. The first approach is by developing immunotherapies for viral infections. Currently, we plan to develop IAP0971 for HBV infection, and submit an IND application for a Phase I trial in the second quarter of 2024. We will continue exploring immunotherapy regimen for the treatment of viral infection through modulating innate or adaptive immune responses to microbial pathogens to promote the anti-pathogen immune response or to prevent immunopathology. The second is by developing multi-valent neutralizing antibodies, leveraging our long-acting multi-valent broadly neutralizing antibody platform.

Continue developing our AIM™ Platform to further explore druggability of innate effectors

We will continue developing our AIM™ Platform to harness the potential of innate effectors in cancer treatments. Our focus is on developing antibodies that target different tumor associated antigens and incorporating different cytokines and other immune modulators into multispecific molecules to further enhance the function of innate effector cells. We will also explore different structural formats, and evaluate them in terms of expression, target binding, *in vitro* and *in vivo* biological activities, as well as developability profiles.

Expanding our GMP-compliant manufacturing facility to enhance our production capabilities and starting to assemble our commercial team

As of the Latest Practicable Date, we have three 200L production lines and one 1,000L production line for GMP-compliant drug substance manufacturing for performing preclinical study, pilot production, and conducting early stage clinical trials, as well as commercial-scale drug product lines for liquid injection and lyophilized powder that fulfill different dosage forms. We have completed the installation of a production line for 5,000L bioreactor capacity, and completed the qualification in November 2023. When putting into practice, it will enable us to manufacture our drug candidates for Phase III clinical trials and commercialization in-house.

Our commercialization strategy is to first capture market share in China followed by a gradual penetration into other target markets such as the U.S. As our drug candidates approach late clinical stage and commercialization, we intend to form our in-house core commercialization and distribution team by recruiting senior-level sales and marketing personnel who are experienced in treatment fields we focus on. We may also seek strategic collaboration opportunities for the commercialization of our drug candidates in China. In particular, we may selectively license-out, establish joint ventures or through other forms of partnerships collaborate with leading biopharmaceutical companies for executing late-stage clinical trials and/or marketing our drug candidates. The collaboration is expected to bring access to strong distribution channels, high-performing sales team, and long-term relationship with domestic players.

Actively seeking international collaboration opportunities to maximize value of our assets and increase brand awareness on a global scale

We are executing a global registration strategy for our immunocytokine candidates, and will continue implementing a global registration plan for our product candidates. We recognize that partnerships will be a critical source to complement our internal resource and enable us to fully execute our global strategy. As such, we will actively seek collaboration opportunities with international leading pharmaceutical companies to advance clinical trials abroad of our products through out-licensing arrangements. We will also expand our international registration team to secure our global clinical development and registration plan, and strengthen the leading clinical development stage of our featured products, especially our immunocytokine pipeline including IAP0971, IAE0972 and IBB0979.

We have managed to establish our technology platforms and advance multiple candidates into clinical stage through our own R&D capabilities. In the future, we intend to continue enriching our drug portfolio mainly through our internal discovery efforts leveraging our fully-integrated, end-to-end, in-house R&D capabilities to develop biologics. We will continue to focus our in-house discovery efforts on the development of novel immunotherapies especially immunocytokines in furtherance of our current position in this therapeutic development field. We will also build an in-house sales and marketing team focusing on commercializing our products in China once they get approved for marketing by the NMPA.

In the meantime, we aim to proactively enhance our brand awareness worldwide, thereby pave the way for promoting our product candidates and technologies to enter global markets. We believe that raising global awareness of our brand is an important way to promote our product candidates and technologies to enter global markets. As of the Latest Practicable Date, we had applied for 119 patent applications in major jurisdictions around the world. As of the Latest Practicable Date, we had published six papers and abstracts on influential journals, and joined over ten international conferences on cancer therapy. In addition to these ongoing efforts to increase our international presence, partnering with world's renowned pharmaceutical companies will also be a further testament to our R&D capabilities and thereby raise our profile in the pharmaceutical industry. Our current assets have already drawn attention from several MNCs, and we will actively communicate with them for potential collaborations.

Continue to focus on selecting and retaining top talents to fuel our innovation

Innovation is the core growth driver of our business, and talent is the cornerstone of innovation-driven development strategy. We place a high priority on selecting, attracting, and retaining top talent. To fully support our continued growth, we will continue to invest in attracting and retaining top talent in various aspects of our operations, including drug discovery, CMC, clinical development, regulatory affairs, and sales and marketing.

In particular, we plan to recruit more talents specialized in clinical development and sales and marketing of innovative therapeutics. Our robust product pipeline is built with our exceptional drug discovery and development expertise. To further strengthen this competitive advantage, we plan to continue to enhance the capabilities and capacity of our clinical development team both inside and beyond China, in order to advance our clinical development efforts and support regulatory affairs in our target markets.

Moreover, we are committed to the continued development of a cohesive and vibrant corporate culture that inspires and encourages innovation. We will continue to provide our employees with competitive salary package, improved performance evaluation system, and a wide variety of employee development projects, including internal and external training opportunities to help them further improve their technical and management skills.

DRUG CANDIDATES

As of the Latest Practicable Date, we had identified and developed a pipeline of nine products. Our pipeline is featured by our internally developed immunocytokines, which directly modulate both the innate and adaptive immune systems. Our immunocytokine pipeline includes (1) Core Product IAP0971, a dual-moiety, anti-PD-1 antibody-IL-15/IL-15Rα heterodimer dual T cell/NK cell agonist; (2) Core Product IAE0972, a dual-moiety, anti-EGFR antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation; and (3) IBB0979, a dual-moiety, anti- B7 homolog 3 protein ("**B7H3**") antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation. All three products are under clinical development with IND approvals from both the NMPA and the FDA, with IAP0971 and IAE0972 completed the Phase I clinical trials in July 2023 and IBB0979 in the Phase I/II clinical stage. Based on the Phase I clinical data, IAP0971 and IAE0972 have shown good tolerability and preliminary antitumor activities in patients with advanced solid tumors. We have initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first HNSCC patient and the first CRC patient in July 2023 and December 2023, respectively. For IAP0971, we plan to commence Phase II clinical trials in the second quarter of 2024. For another immunocytokine, IBB0979, we dosed the first patient of the Phase I trial for B7H3-high expressing solid tumors in July 2023 in China and expect to complete the Phase I clinical study of IBB0979 in the fourth quarter of 2024 in China.

In addition to immunocytokines, we have developed candidates in forms of monoclonal antibodies ("**mAbs**"), bsAbs, and fusion proteins, which span across various stages of clinical and preclinical development. Our Core Product IAH0968 is an antibody-dependent cell-mediated cytotoxicity ("**ADCC**") enhanced mAb targeting human epidermal growth factor receptor 2 ("**HER2**") with 100% fucose knock out. Currently, we are conducting Phase II clinical trials in patients with inoperable HER2+ advanced or metastatic BTC and HER2+ metastatic CRC as the first-line treatment.

Except for the above mentioned products, we are also developing five other product candidates, i.e. IBC0966, IBD0333, IAN0982, ISH0988 and ISH0613. IBC0966 is a clinical stage, anti- PD-L1 antibody-signal regulatory protein α ("**SIRPα**") bifunctional fusion protein that simultaneously stimulates both innate and adaptive immunity to achieve strong synergistic effects and induce long-lasting tumor-specific immune responses. As of the Latest Practicable Date, IBC0966 has completed the Phase I clinical trial as a monotherapy for the treatment of advanced malignant tumors in December 2023. We expect to enter Phase II clinical trials in the second quarter of 2024. IBD0333 is an anti-CD24-anti-4-1BB bsAb that simultaneously stimulates both innate and adaptive immunity. We have obtained IND approvals from both the FDA and the NMPA on June 2 and July 10, 2023, respectively. We expect to complete the Phase I study in the third quarter of 2025. IAN0982, ISH0988 and ISH0613 are currently in the preclinical stage. We expect to file IND applications for them in 2024. The following chart summarizes the development status of our Core Products and other selected drug candidates as of the Latest Practicable Date.


Candidate*
MoA
Platform
Regimen
Indication (Line of treatment)
Preclinical
Phase I
Phase II
Phase III
Commercial rights
Upcoming milestone
Cancer Immunotherapy
Viral Infection
Cancer Immunotherapy
Autoimmune Diseases
IAH0968
HER2 (ADCC enhanced mAb)
AEA™
+CapeOX
HER2+ CRC (1L)
Global
Complete Phase IIb in Q4 2024
+GC
HER2+ BTC (1L)
Complete Phase II in Q3 2025
IAP0971
PD-1/IL-15 (Antibody–cytokine fusion protein)
AIC™
Mono
NSCLC (2L)
Enter Phase II in Q2 2024
+Chemo
Non-squamous NSCLC (1L)***
Global
Enter Phase II in Q3 2024
+BCG
BCG-unresponsive high risk NMIBC (2L/3L)
Complete Phase I in Q4 2024
IAP0971
PD-1/IL-15 (Antibody–cytokine fusion protein)
AIC™
+nucleoside analogues
HBV
Global
Enter Phase I in Q3 2024
IAE0972
EGFR/IL-10 (Antibody–cytokine fusion protein)
AIC™
Mono
HNSCC (2L) and CRC (3L)
Complete Phase II in 1H 2026
+Chemo
Squamous NSCLC (2L)***
Global
Enter Phase II in Q3 2024
+Chemo
HCC (1L)***
Enter Phase II in Q2 2024
IBB0979
B7H3/IL-10 (Antibody–cytokine fusion protein)
AIC™
Mono
B7H3-high expressing solid tumors (≥2L)
Global
Complete Phase I in Q4 2024
IBC0966
PD-L1/SIRPα (Bispecific antibody fusion protein)
bsFp platform
Mono
Solid tumors (≥2L)
Greater China**
Enter Phase II in Q2 2024
IBD0333
4-1BB/CD24 (Bispecific immune modulatory antibody)
bsAb platform
Mono
Solid tumors (≥2L)
Global
Complete Phase I in Q3 2025
IAN0982
Confidential (Multispecific innate effector activator)
AIM™
Mono
Solid tumors
Global
IND filing in Q2 2024
ISH0988
Confidential (Anti-inflammatory and tissue protective)
AIC™
Mono
IBD
Global
IND filing in Q2 2024
ISH0613
Confidential (Inhibit B cell activation and IFNα secretion)
AIC™
Mono
SLE
Global
IND filing in Q2 2024
Core Product
NMPA
FDA
Preclinical stage

Abbreviations: 1L = first-line; 2L = second-line; 3L = third-line; ADCC = antibody-dependent cell-mediated cytotoxicity; AEA™ = ADCC Enhanced Antibody Platform; AIC™ = Armed ImmunoCytokine Platform; AIM™ = Armed Innate Effector Multispecific Platform; BCG = Bacillus Calmette-Guerin; bsAb = bispecific antibody; bsFp = bispecific fusion protein; CapeOX= capecitabine and oxaliplatin; Chemo = chemotherapy; FDA = U.S. Food and Drug Administration; GC = gemcitabine and cisplatin; IND = Investigational New Drug; mAb = monoclonal antibody; Mono = monotherapy; NMPA = National Medical Products Administration; NSCLC = non-small cell lung cancer; NMIBC = non-muscle invasive bladder cancer; BTC = biliary tract carcinoma; CRC = colorectal cancer; HBV = hepatitis B virus; HNSCC = head and neck squamous cell carcinoma; HCC = hepatocellular carcinoma; IBD = inflammatory bowel disease; Q1 = first quarter; Q2 = second quarter; Q3 = third quarter; Q4 = fourth quarter; 1H = first half; SLE = systemic lupus erythematosus.

Notes:

* All the product candidates are administered intravenously, except for IAP0971 for the treatment of 2L/3L NMIBC, which will be administered through intravesical instillation, as well as IAP0971 for the treatment of NSCLC, which will be administered through subcutaneous injection.

** We acquired exclusive rights from ImmuneOnco Biopharmaceuticals (Shanghai) Inc. to develop, manufacture and commercialize IBC0966 in Greater China including mainland China, Hong Kong, Macau, and Taiwan, as well as 7.5% of interests in the overseas rights of IBC0966. For more information, see "— Collaboration Arrangement — Collaboration Agreement With ImmuneOnco in Relation to the Development of IBC0966" in this section.

*** We have completed Phase I clinical trials of relevant products as monotherapy, and plan to leverage data collected in the respective trials and directly seek IND approvals from competent regulatory authorities to conduct Phase II clinical trials of relevant products as combination therapy.

Our pipeline products modulate both innate and adaptive immunity to achieve synergistic effect on regulating immune microenvironment.

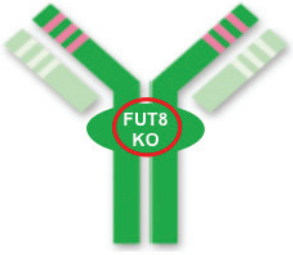
Introduction of Innate and Adaptive Immunity

The immune system comprises two main components: the innate immune system and the adaptive immune system. They are two distinctive immune systems that cooperate to build up an integrated immune response. Innate immunity is a non-specific defense system people are born with. It protects the host against all antigens, yet has no immunologic memory. It includes physical barriers, such as skin and mucosa membrane, innate immune cells, such as phagocytes and NK cells, and immune molecules, such as cytokines. Adaptive immunity, on the other hand, is an antigen-dependent, specific defense mechanism that a body develops to fight foreign molecules. It is able to create immunological memory so that the immune system will be able to respond more rapidly and effectively to pathogens that have been encountered previously. It includes adaptive immune cells, such as T cells and B cells, and immune molecules, such as immunoglobulins.

Simultaneous stimulation of innate and adaptive immunity can achieve a synergistic effect, which will lead to highly efficient recognition and clearance of pathogens. Cytokines, produced by various innate effector cells or adaptive immune cells, are essential in modulating both innate and adaptive immune systems. Antigen presenting cells ("**APC**") act as the bridge between the two systems. They mainly include dendritic cells and macrophages that can phagocytose antigens, degrade them into peptides and display the processed antigen peptides on the cell surface for T cells recognition and secrete cytokines, and thereby initiating the adaptive immune responses. In turn, T cells can stimulate macrophages and NK cells through the release of cytokines to directly kill pathogens. Therefore, when innate and adaptive immunity are both activated, an enhanced and more long-lasting immune response compared to either of them alone will be generated.

Core Product: IAH0968 (ADCC enhanced anti-HER2 mAb)

IAH0968 is a clinical stage, ADCC enhanced anti-HER2 antibody with complete removal of fucose. Removal of fucose from the Fc region of the anti-HER2 antibody moiety enables IAH0968 to bind to the receptor FcγRIIIa with a higher affinity, which will activate the immune system more efficiently comparing to the unmodified anti-HER2 antibody. The diagram below illustrates the structure of IAH0968:



Source: Company data

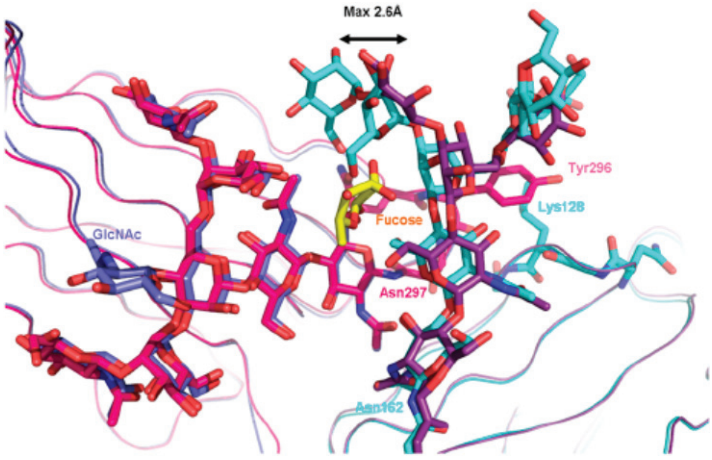
We obtained the IND approval for conducting Phase I and Phase II clinical trials of IAH0968 from the NMPA in October 2020, commenced the Phase I clinical trial in August 2021, and have completed the Phase I clinical trial of using IAH0968 as a monotherapy for heavily pretreated patients with advanced HER2+ malignant solid tumors in March 2023. On September 28, 2022, we received IND approvals from the NMPA for conducting Phase II clinical trials for IAH0968 in combination with gemcitabine and cisplatin in inoperable HER2+ advanced or metastatic BTC as first-line therapy, and Phase II and Phase III clinical trials for IAH0968 in combination with CapeOX (capecitabine + oxaliplatin) in HER2+ metastatic CRC as first-line therapy. We dosed the first patient of the Phase II clinical trial to evaluate IAH0968 in HER2+ metastatic CRC in May 2023 and also dosed the first patient of the Phase II clinical trial to evaluate IAH0968 in HER2+ advanced BTC in August 2023. We completed the Phase IIa trial for CRC in March 2024, commenced a Phase IIb/III trial for CRC in January 2024, and expect to complete the Phase IIb trial in the fourth quarter of 2024. In addition, we also expect to complete the Phase II trial for BTC in the third quarter of 2025.

Mechanism of Action

Antibodies consist of two structural regions, Fab and Fc. Unlike Fab region, which defines the specific pathogen target, Fc region binds to FcR on cell membrane, which could initiate and control cell-mediated effector functions as ADCC, antibody-dependent cellular phagocytosis ("**ADCP**"), and complement-dependent cytotoxicity ("**CDC**"). The stronger the affinity between the Fc region and FcR, the higher the activities of cell-mediated effector functions.

Different approaches have been adopted to achieve enhanced ADCC, mainly including Fc engineering, such as through amino acid alterations (i.e. margetuximab) and fucose removal, to increase the affinity between the Fc region and FcR. Studies of the structure of the Fc region of antibodies and its receptor FcγRIIIa complex revealed that the core fucose of the Fc region is accommodated at a place that interferes with the binding between the Fc region and FcγRIIIa, and thus reducing the affinity between them and resulting in lower ADCC activity. Therefore, modifying to remove fucose is desirable to better recruit immune cells, resulting in enhanced ADCC activity. As a result, this approach has been widely attempted in the biopharmaceutical industry. Fucose removal can be achieved either through the post-expression modification by enzyme digestion or through the construction of new cell lines. However, despite numerous attempts by multiple players to modify antibodies through various approaches, most resulting antibodies still contain a certain percentage of core fucose.

Antibody Core Fucose Increases the Binding Distance Between Fc and Fc Receptor

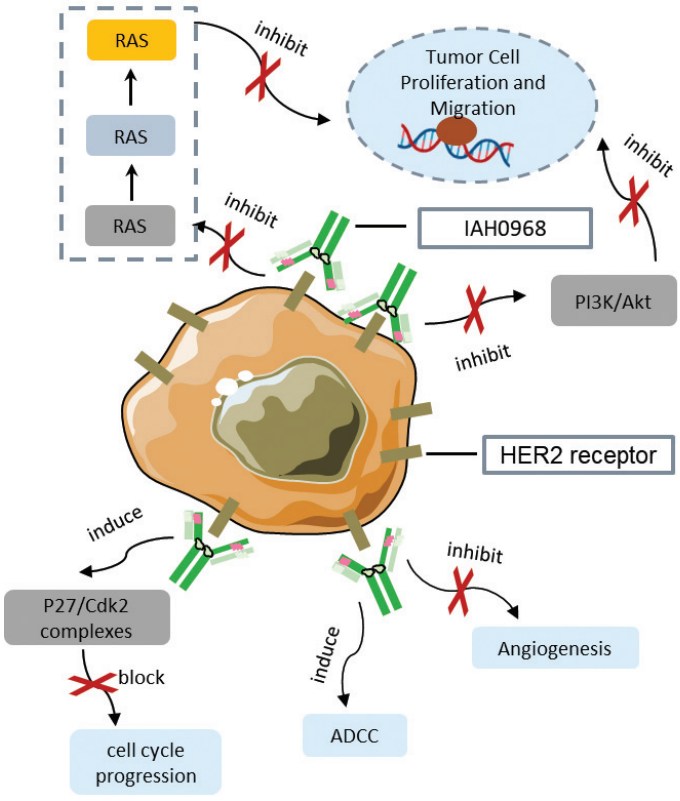


Note: The blue antibody on the right is the antibody with the core-fucose removed, and the purple is normal antibody with core-fucose unmodified.

Source: Ferrara et al., PNAS

HER2 is a validated molecular target for cancer therapy. Over-expression of HER2 has been observed in many cancer types including BTC and CRC. Researches demonstrated that HER2 plays a major role in promoting cell proliferation and suppress apoptosis. Amplification of the HER2 and overexpression of its product may drive excessive or uncontrolled cell growth and tumorigenesis. Antibodies targeting HER2 induce HER2 endocytosis followed by receptor degradation, and as a result constitutively inhibit the activation of the HER2 signaling network and thus inhibits angiogenesis and induces ADCC.

IAH0968 is produced from our proprietary AEA™ Platform. The platform is an internally constructed cell line with mutated FUT8, which encodes α-1,6-fucosyltransferase. α-1,6-fucosyltransferase catalyzes the transfer of fucose from GDP-fucose to the asparagine-linked GlcNAc residue of complex N-glycans via α1-6 linkage. Through biological engineering of FUT8, the cell line will not be able to express α-1,6-fucosyltransferase, and thus proteins generated through the cell line do not carry any fucose. In such a way, we have successfully generated potentially the first complete fucose removal anti-HER2 antibody. Because fucose residue located in the Fc region is also removed, IAH0968 is expected to have enhanced ADCC effect against HER2+ tumor cells.



Source: Frost & Sullivan analysis

Below is a comparison between IAH0968 and other approved anti-HER2 antibodies:

Categories	IAH0968	trastuzumab	pertuzumab
Similarities			
MoA	Binding to the HER2 protein on the surface of tumor cells, blocking tumor cell growth, while simultaneously killing tumor cells through ADCC activity.		
Subtype Class	IgG1	IgG1	IgG1
***In Vivo* Tumor Cell Proliferation Inhibition Activities**	According to our preclinical studies in human breast cancer cell lines of SKBR3 and BT474, and human ovarian cancer cell line SKOV-3, IAH0968 and trastruzumab achieved similar tumor cell proliferation inhibition effect.		Weaker than trastuzumab[1]
Epitope	The binding epitope of IAH0968 and trastuzumab on HER2 is the same, which differs from that of pertuzumab.		
Differences			
Fucose Modification Ratio	0%	76%[2]	97.4%[3]
Fc Receptor Affinity: CD16a（V158）	25.9 nM	275 nM	Similar to trastuzumab[4]
Fc Receptor Affinity: CD16a（F158）	79.3 nM	1560 nM	NA
BT474 158V/V ADCC Activity	Strong (EC_{50}: 17.75ng/ml)	Weak (EC_{50}: 343.7ng/ml)	Similar to trastuzumab[5]
BT474 158F/F ADCC Activity	Yes (EC_{50}: 63.25ng/ml)	No	Similar to trastuzumab[5]
Tumor Growth Inhibition Rate at 5mg/kg	106%	51%	Similar to trastuzumab[5]
MTD in cynomolgus monkeys	>100mg/kg	>25mg/kg[6]	15-50mg/kg[7]

Abbreviations: NA = not available.

Notes:

1 Brockhoff et al., Cell Prolif. 2007, 40, 488-507;

2 Junttila et al., Cancer Res; 70(11) June 1, 2010;

3 Yao et al., BioMed Research International 2022;

4 Boesch et al., MABS 2017, VOL. 9, NO. 3, 455-465;

5 Scheuer et al., Cancer Res 2009; 69: (24);

6 Japan Pharmacology Reviews;

7 FDA Pharmacology Reviews, 2012.

Source: Company data

Market Opportunities and Competition

We are currently investigating IAH0968 for the treatment of BTC and CRC, and plan to further explore its potential in these indications.

BTC

BTC ranks as the second most prevalent type of hepatobiliary cancer globally and primarily encompass cholangiocarcinomas ("**CCAs**") and gallbladder carcinoma. According to Frost & Sullivan, the global market of BTC drugs increased from US$0.5 billion to US$0.7 billion with a CAGR of 10.7% from 2018 to 2022. The number is projected to reach US$1.5 billion in 2026 and US$2.5 billion in 2030 with a CAGR of 21.7% and 13.3% from 2022 to 2026 and from 2026 to 2030, respectively. The China market BTC drugs increased from US$0.2 billion to US$0.3 billion with a CAGR of 7.9% from 2018 to 2022. The number is projected to reach US$0.8 billion in 2026 and US$1.6 billion in 2030 with a CAGR of 28.2% and 17.9% from 2022 to 2026 and from 2026 to 2030, respectively.

In clinical practice, there is a lack of standardized treatment recommendations in the guidelines for HER2+ BTC, which accounts for approximately 20% of BTC patients. In the first-line treatment of BTC, there are no specific drugs recommended for HER2+ BTC, indicating a notable scarcity of treatment options for these patients. While HER2-targeted therapies, such as pertuzumab in combination with trastuzumab, have been recommended for second-line treatment of BTC, the development of drug resistance against HER2-targeted therapies and disease progression remain inevitable challenges.

Therefore, there is an urgent need for novel treatment options to enhance the current BTC treatment landscape. Enhanced engagement of the immune system through ADCC holds significant promise in improving the outcomes of HER2-targeted therapy and should be explored as a potential avenue for advancement. For further details, see "Industry Overview — Immuno-Oncology Drugs Overview — Major Indications for Immuno-Oncology Therapies — BTC" in this document.

CRC

Colorectal cancer ("**CRC**"), also known as bowel, colon, or rectal cancer, refers to cancerous growths that develop in the colon or rectum. According to the Frost & Sullivan, the global market of CRC drugs increased from US$16.2 billion to US$20.6 billion from 2018 to 2022, and is projected to reach US$30.9 billion in 2026 and US$43.7 billion in 2030. The China market of CRC drugs increased from US$1.5 billion to US$2.6 billion from 2018 to 2022, and is projected to reach US$5.0 billion in 2026 and US$7.8 billion in 2030.

Due to a lack of early cancer screening and diagnosis in China, a staggering 89% of clinically diagnosed CRC patients are already in the late stages of the disease. Currently, for late-stage CRC (metastatic disease), chemotherapy alone or in combination with targeted therapies such as bevacizumab and cetuximab (an anti-EGFR antibody) is recommended as the first-line treatment. PD-1/PD-L1 inhibitors, like Keytruda, have only been recommended for a small subset of patients with the MSI-H/dMMR subtype in the first- and second-line treatments.

However, over time, the therapeutic benefits of targeted therapies in combination with chemotherapy, such as bevacizumab and cetuximab, diminish. The median progression-free survival ("**mPFS**") for these treatments ranges from 8.9 to 10.6 months in the first-line and decreases to 4.1 to 7.5 months in the second-line treatment. Patients have limited effective options if the initial treatment with bevacizumab, cetuximab and chemotherapy fails due to drug resistance. Additionally, PD-1 inhibitors, while providing an alternative treatment option for some CRC patients, are only approved for a very small percentage (5%) of patients with MSI-H/dMMR and have not been approved for general use in CRC due to limited overall response rates of less than 10% in clinical trials. Consequently, novel immuno-oncology therapies improving the immune response against tumor cells are needed to address the medical needs in metastatic CRC treatment, especially by enhancing T cells and NK cells activities. For further details, see "Industry Overview — Immuno-Oncology Drugs Overview — Major Indications for Immuno-Oncology Therapies — CRC" in this document.

Competitive Landscape

According to Frost & Sullivan, there are three anti-HER2 mAbs in clinical development for cancer treatment globally. Among them, the most advanced product is in the Phase II/III clinical stage. In China, there are four products in clinical development, with the most advanced ones also in Phase II/III stage. IAH0968 stands out as the only and the most clinically advanced ADCC-enhanced anti-HER2 mAb modified through fucose removal in China and rest of the world, which is currently in the Phase II/III clinical stage.

Competitive Advantages

IAH0968 is potentially the world's first 100% fucose-removed HER2 antibody developed based on our AEA™ Platform. This antibody exhibits enhanced tumor-killing abilities and can potentially be used for the treatment of a wider range of HER2+ tumors.

Advantages in terms of molecular design

IAH0968 is manufactured based on the AEA™ Platform, our proprietary, internally developed FUT8-knock-out cell line, which produces antibodies with 0% core fucose. As a result, because no fucose on the Fc region of the antibody, the antibody will have enhanced ADCC. In contrast, current HER2-targeted therapies such as trastuzumab expressed in FUT8 wild-type cells, which can have more than 90% core fucose residue on the Fc region.

Favorable safety portfolio

Toxicological studies conducted in cynomolgus monkeys have demonstrated that the maximum tolerated dose for a single dose of IAH0968 is 618 mg/kg, and the no observed adverse effect level for repeated doses (doubled for the first dose) is 200/100 mg/kg. These values significantly surpass the converted dose of the validated data for IAH0968 in mice, highlighting the encouraging safety profile of the product candidate.

The favorable safety profile has been validated in both Phase I and Phase II clinical trials. Specifically, in 18 patients who received IAH0968 monotherapy up to 20mg/kg, all patients experienced treatment-related adverse events (TRAEs), with most being Grade 1-2. Only four subjects experienced Grade 3 adverse events (AEs). Additionally, the maximum tolerated dose (MTD) was not reached. A similar safety profile was observed for IAH0968 combination therapy. In 9 patients who received IAH0968 (up to 15mg/kg) in combination with CapeOX, we observed that most TRAEs were Grade 1-2. No dose-limiting toxicities (DLTs) occurred, and the MTD has not been reached.

Superior efficacy portfolio

In a preclinical study, we demonstrated that IAH0968 and trastuzumab exhibit similar binding activities to tumor cells expressing the HER2 antigen, indicating that 100% removal of fucose does not affect the target recognition of IAH0968. In this study, we co-incubated IAH0968 with tumor cells of varying HER2 expression levels (SKBR3, BT474, SKOV3, and A549) and used APC anti-human IgG Fc fluorescent antibody as the secondary antibody to investigate the binding activity of the drugs to the tumor cells. Data showed that the binding activity of IAH0968 to tumor cells is similar to that of trastuzumab.

	Cell Type	IAH0968	trastuzumab
Binding to the surface antigen HER2 on tumor cells. (EC_{50} (μg/ml))	SKBR3	2.315	1.893
	BT474	2.732	2.661
	SKOV3	1.465	1.370
	A549	No binding	No binding

Source: Company data

- IAH0968 exhibits 10-20 times higher affinity for FcγRIIIa compared to trastuzumab, resulting in 5-20 times greater killing activity for ADCC in HER2+ tumor cells. In a mouse subcutaneous tumor model, IAH0968 achieved a 100% tumor growth inhibition rate, surpassing the effectiveness of trastuzumab despite lower dosage.

- IAH0968's ADCC efficacy remains unaffected by FcγR polymorphisms in NK cells and shows significant effectiveness against the 158V/F and 158F/F polymorphisms, which are prevalent in 80% of the population. The Phase I clinical trial has demonstrated that IAH0968 remains effective in patients with trastuzumab-resistant breast and gastric cancers. Additionally, in endline patients with cholangiocarcinoma and colorectal cancer who experienced drug resistance to previous treatments, IAH0968 achieved an ORR of 40% and DCR of 80%.

- In a Phase II clinical trial, IAH0968 demonstrated encouraging preliminary antitumor activities in combination with CapeOX in subjects with HER2+ advanced or metastatic CRC and malignant solid tumors who failed or were resistant to multiple frontline therapies, achieving an ORR of 50% and a DCR of 75%.

Advantages in terms of production

- The production of IAH0968 is enabled by the FUT8-knock-out cell line, which showed exceptional host cell growth and expression characteristics. The cell line can achieve a maximum cell density of 3×10^7 cell/mL. It can maintain stable antibody expression for extended periods and achieving high levels of cell expression at approximately 4g/L. The resulting purification efficiency is also notably high, ensuring the commercial scalability of IAH0968 while maintaining consistent quality.

- The manufacturing process for IAH0968 will utilize 5,000L stainless steel bioreactor for commercial production, further reducing production costs and elevating its market competitiveness.

Summary of Clinical Trial Results

Phase II clinical trial in patients with HER2+ advanced/metastatic CRC

Trial Design. This is an open-label Phase II study of IAH0968 in patients with HER2+ metastatic CRC. This trial is conducting in China. Phase IIa of the study is to evaluate the safety and tolerability of IAH0968 in combination with CapeOX in HER2+ advanced or metastatic malignant solid tumors and to determine the MTD and/or the RP2D of the combination therapy. Phase IIb of this study is to evaluate the efficacy of IAH0968 in combination with CapeOX in HER2+ metastatic CRC by PFS according to RECIST 1.1.

The primary objective of the Phase IIa trial are safety and tolerability. The secondary objective includes PK, anti-drug antibody ("**ADA**"), ORR and PFS. The primary objective of the Phase IIb study is PFS. The secondary objective includes ORR, OS, one year survival rate, DCR, AEs, SAEs and ADA.

Trial Status. The Phase IIa clinical trial of IAH0968 for 1L HER2+ metastatic CRC has been completed in March 2024. We have initiated the Phase IIb study in January 2024.

Safety Profile. As of the data cut-off date (March 11, 2024), patient enrollment for IAH0968 combination therapy has been completed in the 10 mg/kg and 15 mg/kg dose groups. A total of nine subjects received IAH0968 in combination with CapeOX administration during the study, and safety observations were conducted. No DLTs occurred, and the MTD has not been reached.

All nine subjects (100.00%) experienced treatment-related adverse events ("**TRAEs**") during the study, the majority of which were Grade 1-2. The most common TRAE was hypoalbuminemia (9/9), up to Grade 2. Grade 3 TRAEs were experienced by eight subjects (8/9), including diarrhea (3), decreased neutrophil count (2), decreased platelet count (2), asthenia (1), decreased white blood cell count (1), anemia (1) and hypokalemia (1).

Efficacy Profile. As of the data cut-off date (March 11, 2024), eight subjects underwent efficacy assessment. Among them, one subject achieved complete response ("**CR**") on the best response evaluation, three subjects achieved partial response ("**PR**") on the best response evaluation, resulting in an ORR of 50% (4/8). In addition, two subjects achieved SD, leading to a DCR of 75% (6/8). These results demonstrated the preliminary clinical efficacy of IAH0968 in combination with CapeOX in subjects with HER2+ advanced or metastatic CRC and malignant solid tumors who failed or were resistant to multiple frontline therapies. The efficacy of IAH0968 combination therapy during the Phase IIa study is summarized in the table below:

Group	Indication	Previous Treatment	Efficacy
10 mg/kg	Colon cancer with metastases to the liver, abdominal cavity, and supraclavicular lymph nodes	Treated with oxaliplatin + capecitabine; trastuzumab; raltitrexed + pyrotinib; pertuzumab + trastuzumab + irinotecan + calcium folinate + fluorouracil; DP303c; regorafenib; fruquintinib + trastuzumab + sintilimab; disitamab vedotin); trastuzumab + regorafenib; cadonilimab + bevacizumab + trifluridine + tipiracil; all resistant	SD. Achieved SD at first efficacy evaluation after two cycles of IAH0968 treatment, and lasted for six cycles
10 mg/kg	Gastric cancer with lymph node metastasis	Treated with trastuzumab + oxaliplatin + capecitabine followed by capecitabine maintenance regimen; paclitaxel + camrelizumab + apatinib; disitamab vedotin; all resistant	SD, still under treatment for 12 cycles. Achieved SD at first efficacy evaluation after two cycles of IAH0968 treatment, and lasted for ten cycles
10 mg/kg	Breast cancer with right chest wall, sternum, axilla, left supraclavicular fossa lymph nodes and lung metastases	Treated with docetaxel + epirubicin + cyclophosphamide; docetaxel + hesperidin; Gaynor; hesperidin; tamoxifen; disitamab vedotin; pyrotinib + capecitabine; trastuzumab + pertuzumab + gemcitabine + cisplatin; pyrotinib + inetetamab+ paclitaxel; norethindrone + abciximab + inetetamab; all resistant	PR. Achieved PR at first efficacy evaluation after two cycles of IAH0968 treatment, and lasted for four cycles

Group	Indication	Previous Treatment	Efficacy
15 mg/kg	Colon cancer with liver metastasis	Treated with oxaliplatin + fluorouracil + calcium folinate, resistant	CR, still under treatment for ten cycles. Achieved PR at first efficacy evaluation after two cycles of IAH0968 treatment, and lasted for six cycles; achieve CR at the fourth efficacy evaluation, and lasted for two cycles
15 mg/kg	Colon cancer with liver, lung, and peritoneal lymph node metastasis	Treated with oxaliplatin + capecitabine, resistant	PR, still under treatment for ten cycles. Achieved PR at first efficacy evaluation after two cycles of IAH0968 treatment, and lasted for eight cycles
15 mg/kg	Breast cancer with recurrent skin metastasis of left chest wall, left internal mammary lymph node, right axillary lymph node and left chest wall	Treated with cyclophosphamide + epirubicin; anastrozole + letrozole; pyrotinib maleate tablets/placebo + trastuzumab + docetaxel; capecitabine; vinorelbine + herceptin + pertuzumab; TDM-1; TPK-1 + apatinib; trastuzumab + fulvestrant + Ibex; Abemaciclib; all resistant	PR. Achieved PR at first efficacy evaluation after two cycles of IAH0968 treatment, and lasted for four cycles

Note: Cut-off date: March 11, 2024. Efficacy evaluation according to RECIST 1.1.

Source: Company data

Conclusion. The results of the above studies indicated that IAH0968 in combination with CapeOX was safe and well tolerated. The results also demonstrated preliminary efficacy in patients with HER2+ advanced or metastatic CRC and malignant solid tumors who have failed standard therapies. The RP2D was determined to be 15 mg/kg. Phase IIb/III clinical studies can be commenced in accordance with the Company's proposed clinical development plan.

Phase II clinical trial in adult patients with advanced HER2+solid tumors who have failed standard treatment and treatment-naïve patients with advanced/metastatic HER2+ BTC

Trial Design. This is an open-label, randomized, double-blind Phase II study of IAH0968 in patients with HER2+ metastatic BTC. This trial is conducting in China. Phase IIa study of this trial is in adult patients with advanced HER2+ solid tumors who have failed standard treatment. The study is to determine the MTD, DLT and/or RP2D of intravenous IAH0968 in combination with GC regimen (gemcitabine + cisplatin) in adults with advanced HER2+ solid tumors who have failed standard therapy. Phase IIb study of this trial will be conducted in treatment-naïve patients with advanced/metastatic HER2+ BTC. It is designed to study the first-line use of IAH0968 at the RP2D, as determined in the Phase IIa study, in patients with advanced or metastatic HER2+ BTC without systemic therapy, to compare the efficacy of IAH0968 in combination with GC regimen by ORR with that of placebo in combination with GC regimen according to RECIST 1.1.

The primary objective of the Phase IIa trial is safety and tolerability. The secondary objects include PK, ADA, ORR and PFS. The primary objective of the Phase IIb trial is ORR. The secondary objective includes one-year survival rate, PFS, OS, CRR, DCR, AEs, SAEs and ADA.

Trial Status. We have dosed the first patient in August 2023.

Phase I clinical trial in patients with HER2+ advanced solid tumors

Trial Design. This trial was a Phase I, open-label study of IAH0968 in patients with HER2+ advanced solid tumors. This trial was conducted in China. A total of 18 patients were enrolled in this study. Each treatment cycle is defined as 3 weeks, in which IAH0968 will be administered intravenously (IV) on day 1 of each cycle. Tumor assessments will be performed every 6 weeks (i.e., prior to dosing for Cycles 3, 5, 7, etc.). Patients enrolled in this study who do not experience a DLT or other unacceptable toxicity that necessitates permanent discontinuation of investigational product, may continue treatment for up to disease progression, initiation of alternative anti-cancer therapy, lost to follow-up, withdrawal of informed consent, death, or end of study.

The study included two phases: dose escalation and dose extension. The dose escalation study followed the 3+3 scheme. One subject was included in the 6 mg/kg dose group, and then three to six patients with HER2+ advanced solid tumors that failed standard treatment were included in the fixed three dose groups (10 mg/kg, 15 mg/kg and 20 mg/kg). Once RP2D/MTD dose level has been determined, we recruited additional patients to confirm the RP2D/MTD in HER2+ patients who had failed standard therapy. Dosing began with dose level 0 (10 mg/kg Q3W) and proceed to escalated dose levels of 10 mg/kg Q3W, 15mg/kg Q3W, and 20 mg/kg Q3W, successively.

The primary objective of the Phase I trial was to determine the MTD, RP2D of IAH0968 and DLT, AE and SAE. The secondary objective included assessing PK portfolio, and immunogenicity of IAH0968.

Trial Status. The Phase I study of this trial was completed on March 10, 2023. As of cut-off date (June 12, 2023), we were conducting follow-up observations. However, these follow-up observations will not affect the findings and conclusions from the Phase I clinical trial as reported by the principal investigator ("**PI**") of the trial in the clinical research report, nor will they change the fact that the Phase I clinical trial has been completed.

Safety Profile. The safety analyses were summarized from 18 subjects enrolled in the Phase I of IAH0968. Among 18 subjects, all the patients experienced TRAEs, but most AEs were Grade 1-2. Only four subjects experienced ≥ Grade 3 AEs. Also, MTD was not reached.

TRAEs occurring in ≥10% of patients or ≥ Grade 3 TRAEs

	All patients (N=18)	
	All grades, n (%)	**≥Grade 3, n (%)**
Any TRAE	18(100)	4(22.22)
TRAE in ≥10% of patients by preferred term		
Anemia	13(72.22)	0
Hypoalbuminemia	9(50.00)	0
Hyperuricemia	9(50.00)	0
Infusion-related reactions	9(50.00)	1(5.56)
Hypertriglyceridemia	6(33.33)	0
Alanine aminotransferase increased	6(33.33)	0
Blood alkaline phosphatase increased	5(27.78)	0
White blood cell count decreased	4(22.22)	1(5.56)
Platelet count decreased	4(22.22)	0
Aspartate aminotransferase increased	4(22.22)	0
Hypocalcemia	3(16.67)	0
Hypokalemia	3(16.67)	1(5.56)
Hyperglycemia	3(16.67)	0
Hyponatremia	3(16.67)	0
Diarrhea	3(16.67)	0
Gamma-glutamyl transferase increased	2(11.11)	0
Hypercholesteremia	2(11.11)	0
Neutrophil count decreased	2(11.11)	1(5.56)
Nodal tachycardia	2(11.11)	0
Hyperphosphataemia	2(11.11)	0
Fever	2(11.11)	0
Supraventricular tachycardia	1(5.56)	1(5.56)
Arrhythmia	1(5.56)	1(5.56)
Electrocardiogram QT prolonged	1(5.56)	1(5.56)

Abbreviations: TRAE = treatment-related adverse event.

Note: Cut-off date: June 12, 2023. AEs graded according to NCI CTCAEv.5.0.

Source: Company data

Efficacy Profile. As of the data cut-off date (June 12, 2023), the efficacy analyses were summarized based on data collected from 18 subjects enrolled in Phase I clinical trial of IAH0968, with 15 of them being evaluable for efficacy. An evaluable subject was defined as one who had undergone at least one post-baseline tumor assessment. Among the 15 evaluable subjects, two of them showed a PR, while six subjects exhibited SD. The ORR was calculated to be 13.3%, and the DCR was 53.3%. When considering heavily pretreated metastatic CRC and BTC patients, the ORR increased to 40%, with a DCR of 80%. The table provided below presents a summary of the best responses with PR and SD observed in the 15 evaluable subjects who received IAH0968 during Phase I study.

Indication	Group	Patient	Previous Treatment	Efficacy
CRC, CCA	10 mg/kg	Colon cancer, peritoneal metastasis	Treated with oxaliplatin, capecitabine, trastuzumab, irinotecan, raltitrexed, all resistant	SD, still under treatment. Achieved SD in the first efficacy evaluation after 2 cycles of IAH0968 treatment, and lasted for more than 12 months
	15 mg/kg	Rectal cancer, lung metastasis, pelvic metastasis	Treated with EGFR monoclonal antibody, irinotecan, calcium folinate, fluorouracil, all resistant	PR, still under treatment. After 2 cycles of IAH0968 administration, the subject achieved partial response PR at the first efficacy evaluation. The duration of PR exceeded 12 months, and the tumor volume continued to shrink

Indication	Group	Patient	Previous Treatment	Efficacy
		CCA, liver metastases	Treated with Nab-paclitaxel, capecitabine, all resistance	PR. The subject achieved SD at the first efficacy evaluation after 2 cycles of IAH0968 administration, and then achieved PR at the fourth cycle evaluation. The DCR duration was 3 months, and the tumor volume continued to shrink
		Rectal cancer, liver, perianal metastasis	Treated with Radiotherapy, oxaliplatin, capecitabine, Herceptin, irinotecan, raltitrexed, pirotinib, all resistant	SD. The subject achieved SD in the first efficacy evaluation after 2 cycles of IAH0968, and lasted for 5 months
BC, GC	10 mg/kg	BC, liver, lung, lymph node metastases	Treated with Docetaxel, trastuzumab, pertuzumab, all resistant	SD, still under treatment. The subject achieved SD at the first efficacy evaluation after 2 cycles of IAH0968 administration, and lasted for more than 20 months, and the tumor volume continued to shrink
		GC, lung, lymph node metastasis	Treated with Oxaliplatin, capecitabine, trastuzumab, irinotecan, apatinib, SHR-1701, nab-paclitaxel, all resistant	SD. The subject achieved SD in the first efficacy evaluation after 2 cycles of IAH0968 and lasted for 5 months, and the tumor volume continued to shrink

Indication	Group	Patient	Previous Treatment	Efficacy
	20 mg/kg	GC, liver metastases	Treated with Trastuzumab, oxaliplatin, capecitabine, Tegafur, albumin-paclitaxel treatment, all resistant	SD. The subject achieved SD in the first efficacy evaluation after 2 cycles of IAH0968, and lasted for 4 months, and the tumor volume continued to shrink
		BC, lung metastases	Treated with Pyrotinib Tablets, Trastuzumab, Docetaxel, all resistant	SD. The subject achieved SD in the first efficacy evaluation after 2 cycles of IAH0968, and lasted for 4 months

Source: Company data

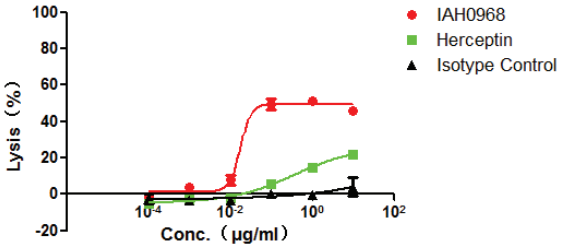
Conclusion. IAH0968, as a monotherapy, demonstrated a favorable safety profile and encouraging preliminary efficacy in individuals diagnosed with HER2+ advanced solid tumors and failed multiple prior therapies within a dose range of 6 mg/kg to 20 mg/kg.

Summary of Preclinical Data

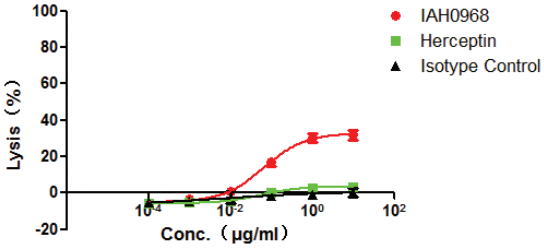
In vitro assays demonstrated that IAH0968 mediated stronger ADCC killing toxicity against HER2+ tumor cells SKBR3, BT474 and SKOV3 than trastuzumab. HER2 high expression breast cancer cell line BT474 was selected as target cells. FcγRIIIa-158V-F polymorphism is located in the extracellular membrane-proximal domain which is considered crucial for antibody binding. NK-92MI-CD16a overexpressing CD16a 158V/V (Fc high affinity receptor) or cells overexpressing 158F/F (Fc low affinity receptor) were effector cells. BT474 cells were collected and put into 96-well plates, and then NK-92MI-CD16a cells overexpressing CD16a 158V/V or CD16a 158F/F were added to each well. IAH0968 or trastuzumab (Herceptin) was diluted in series and added to the plate.

The results showed that IAH0968 could mediate ADCC activity against BT474 in the presence of effector cells NK-92MI-CD16a (158V/V) or NK-92MI-CD16a (158F/F). The ADCC activity was stronger than trastuzumab or Herceptin. Herceptin could not mediate the ADCC activity against BT474 in the presence of effector cells NK-92MI-CD16a (158F/F).

Tumor Cell Lysis by NK Cells Overexpressing CD16a 158V/V



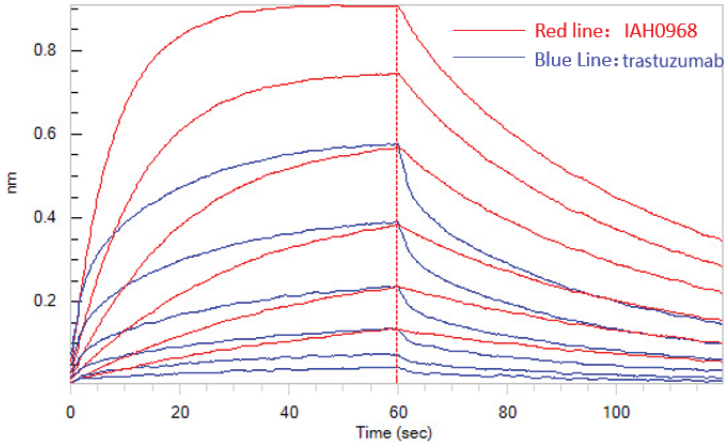
Tumor Cell Lysis by NK Cells Overexpressing CD16a 158F/F



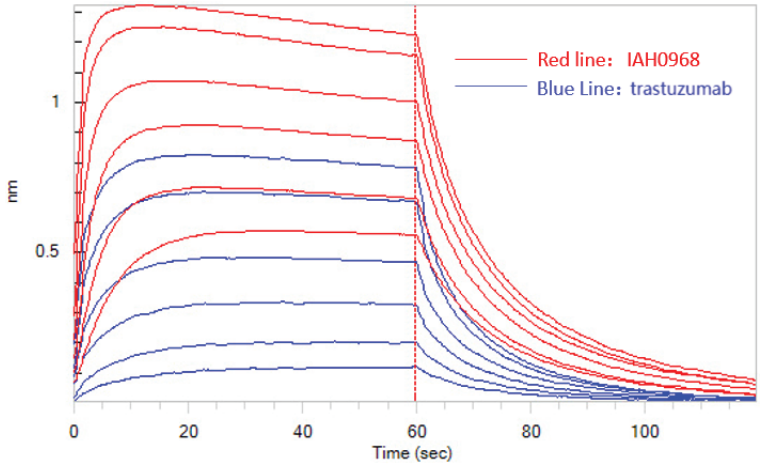
Source: Company data

The binding affinity of IAH0968 and trastuzumab to FcγRIIIa allotypes (158-V and 158-F) was measured. The result showed that IAH0968 increased the binding affinity up to 20-fold comparing to trastuzumab.

Affinity Assay Results of IAH0968 and Trastuzumab with Human CD16a (158-V)

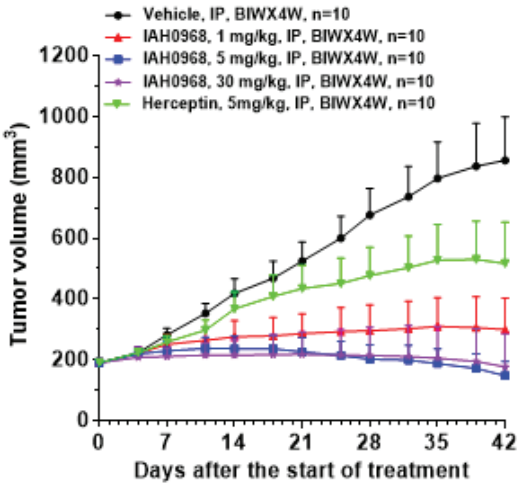


Affinity Assay Results of IAH0968 and Trastuzumab with Human CD16a (158-F)



Source: Company data

An *in vivo* pharmacodynamics study was conducted to evaluate the effects of IAH0968 on a transplanted tumor model using the human breast cancer cell line BT474. The data obtained from the study demonstrated that IAH0968 effectively inhibited tumor growth in mice with BT474 Balb/c subcutaneous transplantation tumors at all three dose levels, and a clear dose-dependent effect was observed. Particularly, at the 5 mg/kg dose and even lower doses (1 mg/kg), IAH0968 exhibited superior efficacy in suppressing tumor growth compared to the control group treated with trastuzumab.



Source: Company data

Safety pharmacology tests demonstrated that a single intravenous injection of IAH0968 at doses ranging from 30-120 mg/kg did not significantly affect the central nervous system function of Sprague Dawley rats. Similarly, intravenous administration of IAH0968 at doses ranging from 30-200 mg/kg had no drug-related effects on body temperature, respiratory parameters, electrocardiogram, and blood pressure in cynomolgus monkeys.

Furthermore, no drug-related toxicity was observed in cynomolgus monkeys (at a dose of 618 mg/kg) and rats (at a dose of 824 mg/kg) after a single administration of IAH0968. With repeated administration of various doses, no immunotoxicity, local irritation, or immunotoxicity was observed in cynomolgus monkeys. The no observed adverse effect level for repeated administration of IAH0968 was determined to be 200/100 mg/kg (twice the initial dose), which significantly exceeded the equivalent effective dose of IAH0968 in mice.

Clinical Development Plan

We are implementing a comprehensive clinical development plan that focuses on a wide range of cancer indications for our IAH0968.

Fast-to-Market Strategy

Our business development plan for IAH0968 includes a fast-to-market strategy of conducting Phase II clinical trials of IAH0968 for HER2+ advanced solid tumors where effective treatment options are scarce or limited, particularly BTC. Our rationale behind these strategic choices is to expedite the regulatory approval process and facilitate the commercial launch of IAH0968.

- 1L HER2+ BTC

According to Frost & Sullivan, there were approximately 63.5 thousand new cases of 1L HER2+ advanced BTC globally in 2022, and the number is projected to reach 84.2 thousand in 2030. In 2022, there were approximately 25.1 thousand new cases of 1L HER2+ advanced BTC in China, and the number is projected to reach 33.1 thousand in 2030. For late stage BTC, the five-year survival rate can be extremely low, at approximately 2%.

BTCs have a poor prognosis due to widespread metastasis and high recurrence rates. Surgery is the primary curative treatment option, but it is only suitable for a small fraction of patients (around 30%) based on the location of the primary tumor. Patients with advanced or unresectable disease rely on chemotherapy, targeted therapy, and immunotherapy. In clinical practice, there is lack of systematic treatment recommendation in the guideline for HER2+ BTC, which accounts for around 20% of BTC patients. In the first-line treatment of BTC, there is no specific drug recommended for HER2+ BTC, indicating a certain lack of treatment options for HER2+ BTC patients.

Our Phase I clinical trial indicated a PR with IAH0968 monotherapy in a heavily pretreated patient with BTC. Namely, a heavily pretreated CCA patient with liver metastases achieved SD at the first efficacy evaluation after two cycles of IAH0968 administration, and then achieved PR at the fourth cycle evaluation. The DCR duration was three months, and the tumor volume continued to shrink.

Given the unmet therapeutic need for HER2-targeted agents in BTC and the potential of IAH0968, we dosed the first patient of a Phase II trial in August 2023 to evaluate the combination of IAH0968 with gemcitabine plus cisplatin as first-line treatment for HER2+ advanced BTC. We plan to submit a BLA of IAH0968 for the treatment of 1L HER2+ advanced BTC to the NMPA in the second half of 2025.

Major Indication

In addition to its potential application in BTC, we are actively assessing the therapeutic efficacy of IAH0968 in the treatment of various other major HER2+ advanced solid tumors, especially CRC.

- 1L HER2+ CRC

CRC is the third most common cancer and the second leading cause of cancer-related deaths globally. According to Frost & Sullivan, there were approximately 50.5 thousand new cases of 1L HER2+ advanced CRC globally in 2022, and the number is projected to reach 64.6 thousand in 2030. In 2022, there were approximately 12.3 thousand new cases of 1L HER2+ advanced CRC in China, and the number is projected to reach 16.0 thousand in 2030. Despite advancements in metastatic CRC treatment, five-year survival rates remain low. For late stage CRC, the five-year survival rate can be approximately 16%. Chemotherapy is the primary treatment, and targeted therapies are limited. HER2 amplification occurs in around 5% of metastatic CRC cases, and clinical trials have demonstrated significant benefits of HER2 blockade in these patients.

On January 19, 2023, the FDA approved the combination of tucatinib and trastuzumab for adult patients with RAS wild-type, HER2+ unresectable or metastatic CRC that has progressed after previous fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy. However currently, there is no specific drug recommended as standard therapy or first-line treatment of HER2+ CRC. In our Phase I clinical trial, IAH0968 monotherapy showed one PR and two SD, resulting in a DCR of 75% among heavily pretreated CRC patients.

Considering the unmet need in CRC and the potential of IAH0968, we dosed the first patient of a Phase II trial in May 2023 to evaluate the combination of IAH0968 with CapeOX (Capecitabine-Oxaliplatin) as first-line treatment in HER2+ advanced CRC patients, and completed patient enrollment in October 2023. We completed the Phase IIa trial in March 2024, and initiated a Phase IIb/III trial in January 2024. We plan to complete the Phase IIb trial in the fourth quarter of 2024, and complete the Phase III trial in the first half of 2026.

Global Strategy

We have formulated a comprehensive global strategy for the clinical development of IAH0968. Leveraging the data collected from the Phase I and Phase II trials, we plan to submit an IND application for IAH0968 in the treatment of selected indications to the FDA in the fourth quarter of 2024. This crucial step will signify our commitment to advancing the development of IAH0968 and bringing a potential therapeutic option to patients worldwide.

Licenses, Rights and Obligations

IAH0968 was developed by us, and we maintain the global rights to develop and commercialize this drug candidate.

Material Communications with Competent Authorities

The material communications with the relevant competent authorities on all ongoing and completed clinical trials in respect of the Core Product IAH0968 are as follows:

- In October 2020, we received the IND approval from the NMPA for conducting Phase I and Phase II clinical trials of IAH0968 in patients with advanced HER2+ malignant solid tumors.

- In September 2022, we received the IND approval from the NMPA for conducting Phase II clinical trials for IAH0968 in combination with gemcitabine and cisplatin in inoperable HER2+ advanced or metastatic BTC as first-line therapy.

- In September 2022, we received the IND approval from the NMPA for conducting Phase II and Phase III clinical trials for IAH0968 in combination with CapeOX (capecitabine + oxaliplatin) in HER2+ metastatic CRC as first-line therapy.

- In September 2023, we conducted an interview with a senior examiner of the NMPA with the attendance of professional parties, which reconfirmed, amongst others, that the Phase I clinical trial of IAH0968 has been completed, and based on the safety and efficacy data from the Phase I clinical trial, that the NMPA had no objection for us to commence the above mentioned Phase II clinical trials of IAH0968.

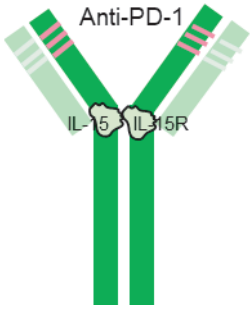
- In December 2023, we conducted a phone interview with the Director of Nanjing Inspection Branch, Jiangsu Provincial Medical Products Administration, which is a provincial branch regulated by the NMPA, with the participation of professional parties (the "**Regulatory Phone Interview**"). During the Regulatory Phone Interview, the Director confirmed that approval of drugs is managed by the approval number, which corresponds to the registration certificate of a drug, and the approval will encompass any different indications or combination therapy approved for marketing. In addition, if there are new indications or combination therapy for a marketed drug, the company can also make a supplemental application, but the company will not receive a new approval number for the same drug. Therefore, the monotherapy and combination therapy of the same drug for different indications, once approved by the NMPA, will be regulated under the same drug certificate in China.

We have not received any concerns or objections from the NMPA related to receiving IND approvals, conducting Phase II clinical trials, or executing any other clinical development plans as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IAH0968 SUCCESSFULLY

Core Product: IAP0971 (PD-1/IL-15 antibody-cytokine fusion protein)

IAP0971 is a clinical stage, dual-moiety, anti-PD-1 antibody-IL-15/IL-15Rα heterodimer dual T cell/NK cell agonist. It is expected to target the PD-1/PD-L1 signaling pathway to relieve the immunosuppression in the tumor microenvironment ("**TME**"), and in the meantime deliver IL-15 to the tumor, and thus locally activates and enhances antitumor functions of CD8+ T cells and NK cells. The diagram below illustrates the structure of IAP0971:



Source: Frost & Sullivan Report

We implement a global registration strategy for IAP0971. IAP0971 received IND approvals for conducting Phase I and Phase II clinical trials in patients with advanced malignant tumors from both the NMPA and the FDA in January 2022 and December 2021, respectively. The Phase I clinical trial in patients with advanced malignant tumors in China was commenced in June 2022, and has been concluded in July 2023. In addition, we obtained the IND approvals of IAP0971 from the NMPA and the FDA in May 2023 and August 2023, respectively, to conduct Phase I and Phase II clinical trials using IAP0971 monotherapy or in combination with Bacillus Calmette-Guerin ("**BCG**") for high risk BCG-unresponsive NMIBC. We plan to commence a Phase II clinical trial for 2L NSCLC in the second quarter of 2024 and enter a pivotal Phase II clinical stage for BCG-unresponsive NMIBC in the fourth quarter of 2024.

Mechanism of Action

PD-1 immunotherapy is the front-line treatment for many cancer types but with unsatisfactory efficacy in immunosuppressed tumors

An important function of the immune system is its ability to differentiate normal cells from foreign objects (such as germs and cancer cells) so that the immune system will attack foreign objects only without harming normal cells. Part of how the immune system does this is by using "checkpoint" proteins on immune cells. The checkpoints act like switches that need to be turned on or off to start an immune response.

PD-1 is a checkpoint protein on T cells, NK cells, and other types of immune cells. It normally acts as a type of "off switch" that helps keep the T cells from attacking normal cells in the body. It turns off the immune system attacks when it attaches to PD-L1, a protein usually found on antigen presenting cells. When PD-1 interacts with PD-L1, it essentially signals the T cell to refrain from attacking the adjacent cell. But cancer cells sometimes also express PD-L1 on their cell surface in large amounts, which helps them evade attacks from the immune system. mAbs that target either PD-1 or PD-L1 can block this binding and boost the immune response against cancer cells.

There are several PD-1 inhibitors approved by the FDA, including Keytruda, Opdivo and Libtayo. Despite their considerable potential for treating certain cancers, drugs targeting PD-1 still present drawbacks including the substantial number of unresponsive patients and patients showing recurrences, represented by relatively low overall response rate. These drawbacks highlight the need for further improvement of anti-PD-1 therapy.

Cytokine monotherapy can be highly toxic to human body while immunocytokines potentially reduces the systemic toxicity of cytokines

Cytokines are small immunomodulating proteins produced by a broad range of cells, which play an important role in cell signaling to modulate the human immune system. They have long been considered a potential candidate for developing immunotherapy that could reverse the immunosuppressive TME. However, there are several major technical obstacles that greatly hinder its druggability, including short half-life due to its relatively low molecular weight and fast degradation (usually below 30kDa), narrow therapeutic window due to strong agonist effects, and systemic toxicity due to off-target delivery. Therefore, engineering cytokines to have improved therapeutic effects and safety has emerged to address these difficulties.

Immunocytokines demonstrate potential to overcome these challenges. They share a structure in form of an antibody-cytokine fusion protein, which consists of a cytokine moiety fused to a monoclonal antibody or to an antibody fragment. Therefore, they are capable of performing dual functions of preferentially localizing the cytokines on tumor lesions and activate antitumor immunity at the site of disease, and in the meantime increasing the half-life of cytokine through linkage to an antibody moiety. As such, this design can potentially increase the therapeutic window and reduce the systemic toxicity of cytokines.

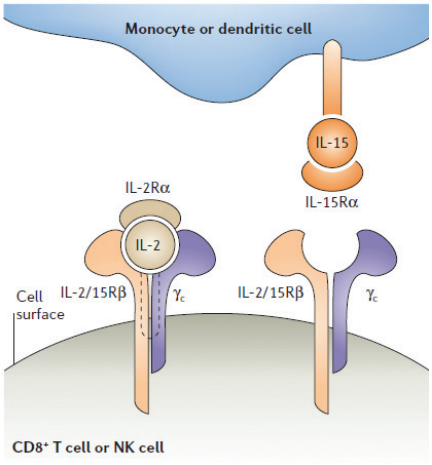
IAP0971, an IL-15-based immunocytokine may provide improved antitumor activity with lower safety risks

Cytokines include several subcategories, including interferons, interleukins and lymphokines. IL-15 is a type of interleukin. It plays a vital role in the regulation of lymphocytes, especially in form of IL-15/IL-15Rα complex. It promotes the proliferation of NK/T cells and inhibits activation-induced cell death of T cells, which can improve the T cell infiltration in tumor tissues and thus potentially address the issues of immune desertification and intrinsic resistance of immunotherapy. IL-15 binds to its receptor IL-15Rα, which

facilitates IL-15 trafficking through the cytoplasm and presentation of IL-15/IL-15Rα complexes on the cell surface. Then, it binds to a receptor complex composed of the IL-2/IL-15Rβ/γ subunits, which are highly expressed on CD8+ T cells and NK cells, to promote the proliferation of NK or T cells.

IL2, the initial cytokine employed in tumor immunotherapy, which has been developed and marketed as cytokine-based therapies like Ontak® and Proleukin®, exhibited promising outcomes in early clinical trials. However, its effectiveness and safety are closely tied to its high affinity receptor, IL2Rα. This receptor, which is predominantly found in Treg cells, competes with T cells for IL-2 binding. Consequently, IL2 exhibits limited efficacy at lower doses and can induce vascular leakage syndrome as a side effect at higher doses.

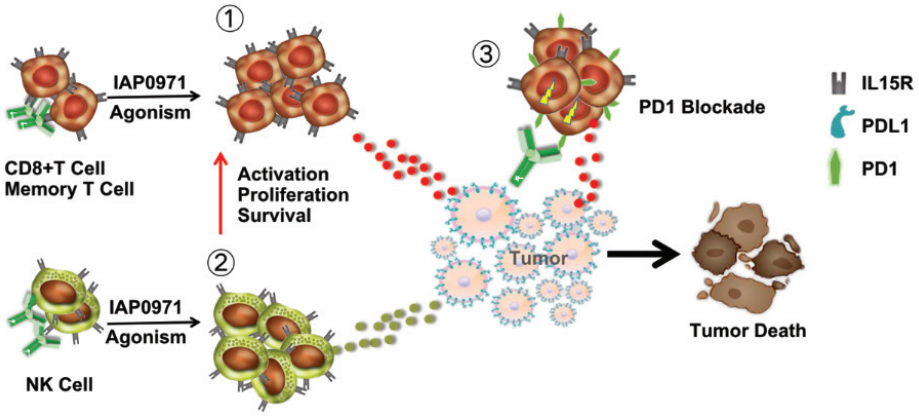
In comparison to IL-2, IL-15 or IL-15-based therapies have not been approved as standalone drugs for distinct clinical use. However, IL-15 possesses structural similarities to IL-2 while offering several unique advantages, making it a potential better candidate for developing cytokine-based therapies. In addition to stimulating immune responses through inducting the proliferation and survival of T cells and promoting the proliferation and differentiation of NK cells, unlike IL-2, it does not promote activation-induced cell death of T cells, and does not promote the maintenance of Tregs, which play the function of suppressing immune response, thereby maintaining homeostasis and self-tolerance. These advantages made IL-15 ranked the first for having the greatest potential for use in cancer immunotherapy by US National Cancer Institute in 2008.



Feature	IL-2	IL-15
Structure	15.5KD, 133AA,4-helix	14-15KD,114AA,4-helix
Producer	Activated T cells	DCs, Macrophages, and Stromal cells
Receptor	IL-2Rα,IL-2Rβ, IL-2Rγ on activated T and B cells	IL-15Rα,IL-2Rβ, IL-2Rγ; DC and Monocytes express IL-15Rα which presents IL-15 to IL-2Rβ, IL-2Rγ expressed on CD8+ T cells and NK cells
Function	Proliferation and differentiation of NK, T and B cells; Treg maintenance and promote AICD (activation-induced cell death) of T cells	Maintenance of CD8+ memory cells and NK cell development; Inhibit AICD of T cells

Source: Thomas Waldmann, Nature Review Immunology, and Company data

IAP0971 is an anti-PD-1 antibody-IL-15/IL-15Rα heterodimer dual T cell and NK cell agonist. It consists of an intact PD-1 antibody and a IL-15/IL-15Rα heterodimer, with the IL-15/IL-15Rα heterodimer being engineered to partially embed into the "hinge" region in the anti-PD-1 antibody. The partial embedded design is expect to balance the activity between PD-1 and IL-15 and to prevent degradation. The heterodimer of IL-15/IL-15Rα utilizes the natural pairing of IL-15 with IL-15Rα together with adopting a knobs-into-holes structure in the Fc region for better heterodimer formation. The anti-PD-1 antibody can thus protect IL-15 from hydrolysis by proteases, decrease the IL-15 activity by steric hindrance, and prolong the half-life of IL-15 without interfering with its target specificity. In addition to this special "protection" function, the anti-PD-1 antibody plays its role as an immune checkpoint inhibitor and blocks the PD-1/PD-L1 signaling pathway to enable T cells to recognize and kill tumors. Specifically targeted to tumor cells by the anti-PD-1 antibody, IL-15 is expected to stimulate CD+8 T cells and NK cells in the local TME without causing systemic cytotoxicity. As such, IAP0971 is expected to be a potent immune system stimulator that can activate both innate and adaptive immunity.



Source: Company data

Similarities and Differences of the Antibody Moiety of IAP0971 Compared to Marketed Anti-PD-1/PD-L1 Antibodies

IAP0971, as an antibody-cytokine fusion protein, comprises both an anti-PD-1 antibody moiety and an IL-15/IL-15Rα complex. In terms of mechanism of action, the anti-PD-1 antibody moiety of IAP0971 functions similarly to marketed anti-PD-1/PD-L1 antibodies by blocking the PD-1/PD-L1 signaling pathway to alleviate T cell immunosuppression. However, structurally, IAP0971 diverges as its heavy chains are distinct, forming a heterodimer through natural pairing, with each heavy chain accommodating either IL-15 or IL-15Rα to form a complex, and through knobs-into-holes mutations on the Fc region, unlike homodimeric monoclonal antibodies on the market. Functionally, IAP0971's anti-PD-1 antibody moiety collaborates with the IL-15/IL-15Rα complex in cis to not only relieve immune suppression but also expand and activate T cells and NK cells, contrasting with other anti-PD-1/PD-L1

antibodies that solely mitigate immune suppression without inducing immune cell expansion, potentially rendering them ineffective against "cold" tumors. For details of the similarities and differences of the antibody moiety of IAP0971 and marketed anti-PD-1/PD-L1 antibodies, see the table below:

A Comparison of the Antibody Moiety of IAP0971 with Marketed Anti-PD-1 and Anti-PD-L1 Antibodies

Categories	IAP0971	Marketed Anti-PD-1 Antibodies			Marketed Anti-PD-L1 Antibodies		
	Anti-PD-1 Antibody Moiety of IAP0971	pembrolizumab	nivolumab	cemiplimab	atezolizumab	avelumab	durvalumab
Similarities							
MoA of the Antibody or Antibody Moiety	Bind to PD-1 protein to block the PD-1/PD-L1 signaling pathway and restore the T cell function from immunosuppressive state.				Bind to PD-L1 protein to block the PD-1/PD-L1 signaling pathway and restore the T cell function from immunosuppressive state.		
Subtype Class	IgG4	IgG4	IgG4	IgG4	IgG1 with glycosylation mutation	IgG1	IgG1 with amino acid alterations
ADCC Effects	No	No	No	No	No	Strong	No
Differences							
Structure	Heterodimer: each of the two heavy chains contains either a IL-15 molecule or IL-15Rα molecule, which will naturally form a IL-15/IL-5Rα complex. The heavy chains also have "knobs-into-holes" amino acid changes.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.
Antitumor Mechanism	Except for the antitumor effect exerted through blocking the PD-1/PD-L1 pathway, anti-PD-1 antibody moiety is expected to have cis-synergistic effect with IL-15/IL-15Rα complex, expanding and activating T cells and NK cells.	No T cells and NK cells expansion function	No T cells and NK cells expansion function	No T cells and NK cells expansion function	No T cells and NK cells expansion function	No T cells and NK cells expansion function	No T cells and NK cells expansion function
***In Vivo* Efficacy Comparison**	In a head-to-head *in vivo* study in MC38-hPD-L1 C57BL/6 hPD1 mice model, IAP0971 demonstrated significantly improved antitumor effect.	No head-to-head comparison available					

Source: Company data

Market Opportunities and Competition

Based on the efficacy data obtained from the Phase I clinical trial, we believe in the potential of IAP0971 as a viable treatment option for non-small cell lung cancer ("**NSCLC**"). Consequently, we are actively progressing towards initiating Phase II clinical trials in patients with NSCLC. Moreover, we are also developing IAP0971 for the treatment of non-muscle-invasive bladder cancer ("**NMIBC**"), and obtained the IND approvals for this indication from the NMPA and the FDA in May 2023 and August 2023, respectively. In addition, we also plan to expand indications of IAP0971 from oncology to anti-viral infection field, especially for the treatment of HBV. Therefore, in the event that IAP0971 obtains marketing approval, it has the potential to create significant market opportunities in the aforementioned indications.

NMIBC

NMIBC refers to the papillary malignant tumor of the bladder that is limited to the bladder mucosa and lamina propria without muscle invasion. The global market of bladder cancer drugs was US$3.4 billion in 2018. The number is projected to reach US$9.0 billion in 2026 and US$13.9 billion in 2030. In China, the bladder cancer drugs market was US$0.2 billion in 2018, and is projected to grow to US$0.9 billion in 2026 and further to US$2.2 billion in 2030.

For postoperative transurethral resection of bladder tumor ("**TURBT**") in high-risk NMIBC patients, the first-line treatment in China and the U.S. is BCG intravesical instillation or radical cystectomy. Although BCG therapy can control tumor progression, the five-year recurrence rate is as high as 66%. In addition, BCG therapy has a high incidence of adverse reactions, with 62.8%-75.2% of patients developing local complications such as urinary frequency, urgency, hematuria, cystitis, and systemic complications such as fever and diarrhea.

Immunotherapy such as PD-1/PD-L1 inhibitors have been demonstrated with great efficacy in treating NMIBC patients who failed BCG therapy or relapsed, and Keytruda or pembrolizumab monotherapy is approved by the FDA for BCG-unresponsive, high-risk NMIBC. However, there is no such approved drug in China, and patients are at risk of radical cystectomy. Inevitably, for patients who cannot receive BCG therapy due to the shortage of BCG, or do not respond to or become relapsed/refractory ("**R/R**") of current therapies, treatment options are limited. This indicates a significant unmet need. For further details, see "Industry Overview – Immuno-Oncology Drugs Overview – Major Indications for Immuno-Oncology Therapies – NMIBC" in this document.

NSCLC

NSCLC is any type of epithelial lung cancer other than small cell lung cancer. According to Frost & Sullivan, the global market for NSCLC drugs has witnessed significant growth, expanding from US$44.7 billion in 2018 to US$72.9 billion in 2022. Projections indicate further substantial growth, with the market expected to reach US$120.4 billion in 2026 and US$168.2 billion in 2030. Similarly, the China market for NSCLC drugs experienced remarkable expansion, surging from US$3.9 billion in 2018 to US$8.0 billion in 2022. Forecasts suggest continued growth, with the market projected to reach US$17.1 billion in 2026 and US$23.8 billion in 2030.

According to Frost & Sullivan, the current treatments will not meet this tremendous need for NSCLC treatments. For NSCLC patients with EGFR mutations, drug resistance to targeted therapies needs to be addressed. For EGFR wild type NSCLC patients, current treatment options mainly include chemotherapy alone or in combination with antiangiogenic agents like bevacizumab, or PD-1/PD-L1 inhibitors such as pembrolizumab. Nevertheless overall, there is no recommended treatment for NSCLC patients who has failed the first-line treatment. Although PD-1/PD-L1 inhibitors have become the frontline treatment for the majority of EGFR wild type NSCLC patients, medical needs still exist due to low response rates. For further details, see "Industry Overview – Immuno-Oncology Drugs Overview – Major Indications for Immuno-Oncology Therapies – NSCLC" in this document.

HBV Infection

HBV is an infectious disease characterized by inflammation of the liver. The clinical symptoms include loss of appetite, liver pain, and weakness. Chronic HBV infection can lead to serious health issues, like cirrhosis or liver cancer. According to Frost & Sullivan, the number of people infected with HBV is gradually declining due to the vaccination plan. In 2022, the number of HBV infected patients reached 284.7 million globally, and it is expected to drop to 273.7 million in 2026. Similarly, in China, the number of people infected with HBV is also gradually declining. In 2022, the number of HBV infected patients in China reached 69.2 million, and it is expected to drop to 65.1 million in 2026. Nevertheless, since HBV infection still affect a large group of patients, treatment to control the progress of the disease is still in great needs.

According to Frost & Sullivan, the global market for HBV drugs increased from US$15.6 billion in 2018 to US$19.2 billion in 2022 with a CAGR of 5.3% from 2018 to 2022. The number is projected to reach US$26.8 billion in 2026 and US$45.9 billion in 2030 with a CAGR of 8.7% and 14.4% from 2022 to 2026 and from 2026 to 2030, respectively. There was an overall decrease in the China HBV drug market from US$1.9 billion in 2018 to US$1.6 billion in 2022 due to the significant decrease in the price of commonly used HBV drugs and the impact of the COVID-19 epidemic. However, in 2026, the number is projected to reach US$2.9 billion, representing a CAGR of 15.5% from 2022 to 2026. In 2030, the China HBV drug market is projected to reach US$7.4 billion, representing a CAGR of 27.0% from 2026 to 2030.

Competitive Landscape

According to Frost & Sullivan, currently, there is no IL-15-based immunotherapy indicated for the treatment of cancer approved for marketing worldwide. Globally, there are 14 products under clinical development. Among these products, IAP0971 and the other seven product candidates are IL-15 based immunocytokines. In China, there are seven products currently under clinical development, with the most clinically advanced products in Phase I/II stage. Only three products including IAP0971 are IL-15 based immunocytokines, and IAP0971 is the most clinically advanced immunocytokine in China.

Competitive Advantages

Advantage in terms of molecular design

IAP0971 represents a new generation of cytokine-based antibody therapeutics, being an immunocytokine with a structure of an anti-PD-1 antibody IL-15/IL-15Rα cytokine fusion protein developed through our AIC™ Platform. Unlike existing PD-1 antibodies and cytokine-based therapeutic areas, IAP0971 has several distinct advantages:

- **Cytokine selection**. IL-15 is a naturally occurring modulator of the human immune system. Unlike IL-2, IL-15's effective receptor is expressed exclusively on CD8+ T cells and NK cells, which have more direct immune cell activation and proliferative activity.

  IL-2 exerts its antitumor effects by binding to the IL-2/15Rβ and IL-2/15Rγ receptors shared with IL-15 on effector T cells and NK cells. Low doses of IL-2 are limited in efficacy due to its competitive binding to Treg. High doses of IL-2 have toxic side effects such as vascular leakage syndrome. Therefore, the clinical use of IL-2 was greatly limited due to these limitations.

  Compared to IL-2, IL-15 has a stronger antitumor effect. This is due to the fact that IL-15Rα is not expressed on Treg cells, and thus IL-15 cannot activate Treg cells or cause apoptosis of T cells. Moreover, IL-15, through the combination with its receptor IL-15Rα located on monocytes and DCs, can act on CD8+ T and NK cells. This makes IL-15 a preferred candidate for developing antitumor therapies. The latest clinical trial results support the therapeutic potential and druggability of IL-15 in NMIBC. Anktiva (N-803), an IL-15 superagonist, plus BCG was evaluated in a Phase II/III trial in BCG-unresponsive NMIBC. Data indicated that in a cohort of patients with carcinoma *in situ* for whom previous therapies had failed, the CR rate was 71% (95% CI, 59.6%-80.3%).

- **Structure and location of IL-15**. The IL-15/IL-15Rα complex is utilized to enhance the tissue distribution of IL-15 and form an anti-PD-1 antibody/IL-15 immunocytokine that preferentially targets T cells in the TME. In contrast, IL-15 alone primarily binds to dendritic cells expressing IL-15Rα, resulting in a receptor sink effect and greater activation of NK cells with high IL-2/15Rβγ expression. Therefore, by adopting IL-15/IL-15Rα complex, IAP0971 is expected to have an improved safety profile.

  An intact bivalent anti-PD-1 antibody fused with a IL-15/IL-15Rα by incorporating IL-15/IL-15Rα in the middle of the antibody to optimize the spatial block of the IL-15 heterodimer and reduce its biological activity. This balance of bioactivities of anti-PD-1 antibody and IL-15 heterodimer improves the therapeutic window of IAP0971. As demonstrated by the IAP0971 PBMC proliferation assay, the results showed that equimolar IL-15/IL-15Rα heterodimer alone and IAP0971 proliferated

CD8+ T and NK cells at similar rates, but IAP0971 exhibited a 5-10 fold reduction in proliferative capacity. This suggests that IAP0971 retains the function of IL-15/IL-15Rα with further reduced activity and an improved therapeutic window.

By placing the IL-15/IL-15Rα heterodimer on the two heavy chains of the anti-PD-1 antibody separately, IAP0971 can leverage the natural pairing of cytokine and cytokine receptor to avoid heavy chain mismatch of the antibody. Placing the IL-15/IL-15Rα heterodimer in the "hinge" region of the anti-PD-1 antibody improves its stability and reduces protease degradation. IAP0971 expression up to 4 g/L and stability data for 12 months demonstrate the advantages of this structure in terms of druggability.

- **Selection of antibody and *cis*-synergy between anti-PD-1 antibody and IL-15**. The anti-PD-1 antibody's activity is contingent upon IL-15 signaling. The anti-PD-1 antibody and IL-15 work in tandem to produce a *cis* synergistic effect on immune cells. This approach not only effectively alleviates immune suppression in the TME, but it also enhances lymphocyte activation and proliferation. IAP0971 is more effective than anti-PD-1 antibodies alone and can overcome primary and secondary drug resistance associated with anti-PD-1 antibodies.

  PD-1+ CD8+ T cells are abundant in the TME, making the anti-PD-1 antibody in IAP0971 particularly useful. It not only extends the half-life of IL-15 but also provides targeted delivery to improve the safety and efficacy of IL-15 while reducing side effects. PD-L1, on the other hand, is mainly present in tumor cells or DC and myeloid cells, whereas IL-15 functions on CD8+ T and NK cells. Therefore, only the fusion protein of anti-PD-1 antibody and IL-15 can act at the same location and on the same type of cells, producing a synergistic effect. In contrast, neither the combination therapy of anti-PD-1 antibodies and IL-15, nor the anti-PD-L1/IL-15 immunocytokines acts in the same location and on the same type of cells, which cannot achieve *cis*-synergy. Additionally, the anti-PD-1 antibody blocks PD-1/PD-L1 signaling, effectively relieving immunosuppression in the TME. Our preclinical studies showed that IAP0971 improves the therapeutic window by 40-fold compared to IL-15 fusion protein.

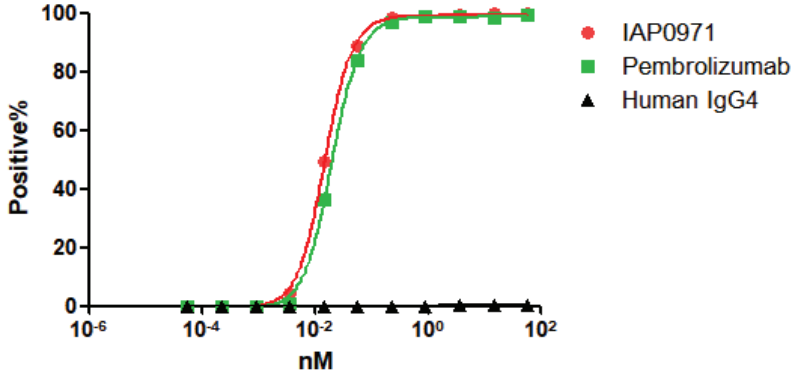
  In summary, the anti-PD-1 antibody moiety of IAP0971 is a humanized variant, the strategic choosing of which for constructing an IL-15 based immunocytokine is driven by several key considerations: Firstly, the combination of anti-PD-1 antibody and IL-15 yields a synergistic effect in *cis*, activating and expanding CD8+ T cells effectively. Secondly, as PD-1+ T cells are predominantly situated in the TME, anti-PD-1 antibodies exhibit heightened efficacy in targeting effector T cells within tumor lesions, thereby exerting a more potent antitumor effect. Thirdly, by incorporating anti-PD-1 antibodies, the issue of IL-15's short half-life can be addressed, leading to its prolonged activity.

- **Structure optimization**. IAP0971 employs the natural pairing of IL-15/IL-15Rα, which leads to more efficient dimerization and eliminates the formation of IL-15 homodimer and half antibody fragments. Additionally, a knobs-into-holes structure is introduced in the Fc region of the anti-PD-1 antibody, further reducing the mismatch of two different heavy chains. These structural designs result in improved productivity of IAP0971.

Our preclinical studies demonstrated the superior efficacy of IAP0971 over standalone anti-PD-1 antibodies, offering potential solutions to the challenges of drug resistance and inefficacy associated with the latter, with its functionalities extensively validated through numerous preclinical studies. These studies encompass assessments such as the efficiency of IAP0971 binding to PD-1 protein and PD-1 overexpressing cell lines *in vitro*, PD-1/PD-L1 blockade assays, PBMC stimulation assays, ADCC assays, and *in vivo* evaluations of antitumor efficacy.

In an *in vitro* preclinical study, binding of IAP0971 and pembrolizumab to PD-1-overexpressing CHO cell line was evaluated by flow cytometry. The results demonstrated that IAP0971 and pembrolizumab showed comparable binding affinity to PD-1.

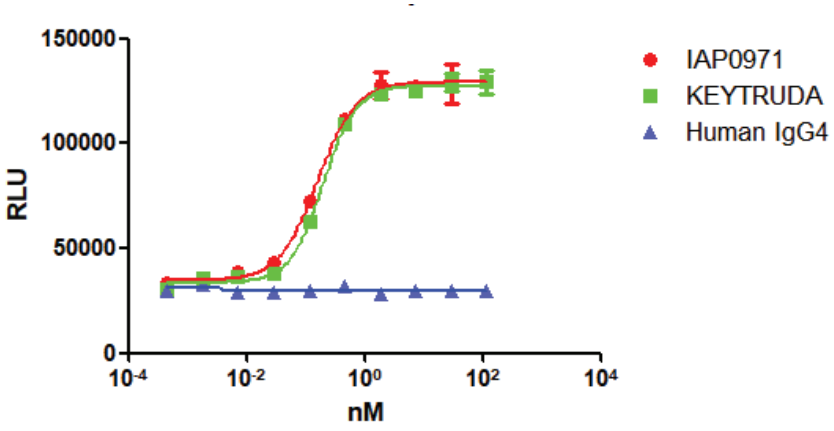
Binding of IAP0971 to CHO-PD-1



Source: Company data

In another *in vitro* preclinical study, Luciferase Reporter assay was used to detect the PD-1/PD-L1 blocking activity of IAP0971. The results showed that IAP0971 can efficiently block the binding of human PD-1 to human PD-L1 and transmit the activation signal of T cells. The blocking activity of IAP0971 was similar to that of pembrolizumab. These results indicated that IAP0971 can release the immune inhibition of PD-1/PD-L1 axis and activate immune effector cells for antitumor activities.

PD-1/PD-L1 Blockade Assay with Luciferase Report

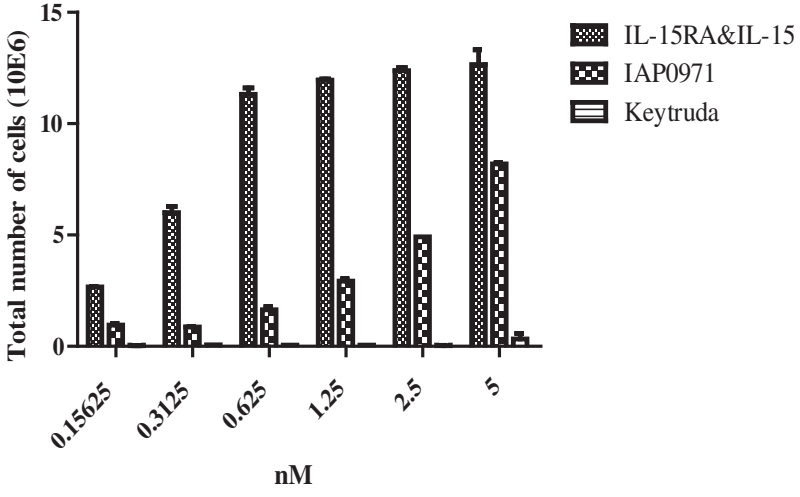


Sample	IAP0971	Pembrolizaumab (KEYRUDA)
EC_{50}(nM)	0.16	0.20

Source: Company data

Our preclinical study also showed that IAP0971 has the PBMC proliferation function. After pre-activation of PBMC with anti-CD3 antibody, stimulation of IAP0971 on PBMC proliferation was detected by the cell counting method. The results showed that IAP0971 and IL-15/IL-15Rα complex could stimulate PBMC proliferation in a concentration dependent manner, which was not observed for pembrolizumab, indicating that the stimulation of IAP0971 on PBMC proliferation depended on the IL-15/IL-15Rα complex in the molecule.

PBMC proliferation-Day12



Source: Company data

Furthermore, our preclinical study showed that IAP0971 was well tolerated and exhibited excellent TGI in MC38-hPD-L1 C57BL/6 hPD1 mice model, superior to the current bestselling anti-PD-1 antibody, Keytruda. For details, see "— Drug Candidates — Core Product: IAP0971 (PD-1/IL-15 antibody-cytokine fusion protein) — Summary of Preclinical Data" in this section.

Although not a head-to-head study, Phase I data also showed that IAP0971 potentially has superior safety and efficacy profiles to N-803, a recombinant IL-15 fusion protein fused with Fc region, indicated for advanced solid tumors when administered subcutaneously.

Phase I data comparison of N-803 and IAP0971

		N-803[1]	**IAP0971**
Registration on ClinicalTrials.gov		NCT01727076	NCT05396391
Indication		Advanced solid tumors	Advanced solid tumors
Route of administration		subcutaneous injection	subcutaneous injection
Dose range		6, 10, 15, 20μg/kg	0.5, 5, 20, 60, 120, 200μg/kg
Dosing frequency		weekly	biweekly
Number of patients		13	15
Safety	Injection site reaction/Infusion related reaction	85%	66.7%
	Hypoalbuminemia	46%	20%
	Anemia	38%	33.3%
	Fever	38%	33.3%
	Lymphocyte count decreased	31%	46.7%
PK		NA	37.08-49.16 hours
Efficacy	Clinical benefits	Single-agent clinical benefit for N-803 was not observed	The disease control rate (DCR) was 36.4%
	NK cell increase	2.3-7.9 fold	22.3-73.7 fold
	CD8 T cell increase	2.7-6.6 fold	9.1-92.3 fold
	CD4 T cell increase	1.6-3.0 fold	4.1-65.4 fold

Abbreviation: NA = not available.

Note:

1. Data for N-803 is from published paper: Clin Cancer Res; 24(22) November 15, 2018.

Source: Company data

As such, IAP0971 has been carefully designed to enhance its biological activity, expand its therapeutic window, optimize its druggability, and improve its production rate. The anti-PD-1 antibody in IAP0971 synergizes with IL-15 to relieve immune suppression in the TME and further activates and proliferates lymphocytes, resulting in a more effective treatment than anti-PD-1 antibodies alone. Additionally, subcutaneous administration of IAP0971 is better tolerated, has a longer half-life than IL-15/IL-15Rα complex Fc fusion protein (N-803), and addresses anti-PD-1 antibody resistance and futility. Overall, IAP0971 is a new therapy for cancer that potentially offers significant advantages over existing treatments.

Favorable safety profile

Based on the preclinical study in cynomolgus monkeys, the half-life of IAP097 spans from 10.5 to 15.7 hours, which is up to approximately two times longer than the half-life of the IL-15/IL-15Rα complex Fc fusion protein (i.e. N-803). In preclinical studies involving repeated subcutaneous dosing of IAP0971 at 1.2 mg/kg, it demonstrated excellent tolerability, surpassing N-803 by nearly 40-fold in dosage. Phase I dose escalation trials have revealed that subcutaneous administration of IAP0971, ranging from 0.5 to 200 μg/kg, was well tolerated by patients and achieved a clinical dose approximately ten times higher than that of N-803.

Superior preliminary efficacy profile

The resistance of anti-PD-1 antibody are mainly attributed to the depletion of immune cells in the TME, and the addition of IL-15 effectively enhances lymphocyte infiltration and numbers in this environment. *In vivo* efficacy data demonstrated that, at the same dose, IAP0971 is significantly more effective than anti-PD-1 antibodies in syngeneic mouse models and remains effective in PD-1-resistant metastatic melanoma models. In the Phase I clinical trial, four heavily pretreated patients including two NSCLC who failed and became resistant to all previous chemotherapy, targeted therapy, immunotherapy, and/or their combination, achieved SD.

Potentially improved efficacy than anti-PD-1 antibodies

The drugability of anti-PD1 antibodies has been thoroughly validated, effectively enhancing efficacy across a wide range of tumors by releasing the brakes on immune checkpoints. However, PD1-targeting antibody drugs still have some limitations, with their efficacy limited to only approximately 20% across various tumor types and facing issues of primary and acquired resistance. Primary resistance is primarily attributed to immune cell desertification in the TME, while acquired resistance is mainly due to immune cell exhaustion. IL-15, on the other hand, can effectively address these two issues. It can efficiently expand and activate CD8+ immune cells, thus addressing the primary resistance issue caused by immune cell desertification. In our preclinical study in the MC38-hPD-L1 C57BL/6 hPD1 mice model, IAP0971 achieved superior tumor inhibition rate (110.47% when treated with 0.5mg/kg of IAP0971 vs. 74% when treated with 0.5mg/kg of anti-PD-1 antibody) and complete tumor regression rate (90% when treated with 0.5mg/kg of IAP0971 vs. 50% when treated with 0.5mg/kg of anti-PD-1 antibody) in our preclinical study.

	IAP0971	An anti-PD-1 antibody
PD-1 binding activity	Similar	Similar
PD-1/PD-L1 blocking activity	Similar	Similar
ADCC activity	No	No
CD8+ T cell and NK cell stimulation activity	Yes	No
Tumor growth inhibition rate at 0.5mg/kg	110.47%	74%
Complete tumor regression rate	90%	50%

Source: Company data

Despite the potential competitive advantages based on the mechanism of action, drug design, preclinical studies, and preliminary clinical data, the successful development of IAP0971 remains highly uncertain, primarily due to the absence of approved IL-15 based immunocytokines. Additionally, whether the anticipated clinical benefits of using anti-PD-1 antibodies in the form of immunocytokines would materialize in targeted patients is still subject to further evaluation and validation in Phase II or later phases of clinical trials.

Summary of Clinical Trial Results

On January 29, 2022 and December 30, 2021, we obtained IND approvals from both the NMPA and the FDA for conducting Phase I and Phase II clinical trials in patients with advanced malignant tumors, respectively. We completed the Phase I clinical trial in July 2023. Based on the Phase I clinical results, upon communication with the principal investigator and without objection from the NMPA, we plan to initiate a Phase II clinical trial for IAP0971 for NSCLC in China in the second quarter of 2024. In addition, we received the IND approval for conducting Phase I and Phase II clinical trials of IAP0971 for NMIBC from the NMPA and the FDA in May 2023 and August 2023, respectively, and dosed the first patient in China in March 2024.

Phase II/III clinical trial of IAP0971 in PD-L1-positive naïve advanced or metastatic NSCLC

Trial Design. This study includes three phases: Phase IIa to evaluate the safety, tolerability and efficacy of IAP0971 for the treatment of subjects with advanced malignant tumors; Phase IIb to evaluate the efficacy of IAP0971 in subjects with driver gene-negative and PD-L1-positive (TPS ≥50%) with naïve advanced or metastatic NSCLC; Phase III to evaluate the efficacy of IAP0971 compared to pembrolizumab for the treatment of subjects with driver gene-negative and PD-L1-positive (TPS ≥50%) naïve advanced or metastatic NSCLC.

Phase IIa of this study is a dose-escalation experiment. We plan to set the starting dose at 400 μg/kg IAP0971, administered every three weeks. The maximum escalating dose is estimated to be at approximately 3000 μg/kg. After the DLT observation is completed in the 3000 μg/kg dose group, we will decide in collaboration with the PI the next step clinical trial design based on whether the MTD is reached considering the collected preliminary safety data.

Phase IIb of this study is a single-arm, open label, multicenter study. 20 to 30 treatment-naïve, driver gene-negative and PD-L1-positive (TPS ≥50%) subjects with advanced or metastatic NSCLC will be enrolled at the RP2D dose determined in Phase IIa. Each treatment cycle will be three weeks until withdrawal or termination.

Phase III of this study is a randomized, parallel-controlled, open label, multicenter study. Driver gene-negative and PD-L1-positive (TPS ≥50%) subjects with advanced or metastatic NSCLC will be enrolled to receive IAP0971 at the RP2D dose established in Phase IIa. Each treatment cycle will be three weeks until withdrawal or termination.

The primary endpoint of Phase IIa of this study is safety. The primary endpoint of Phase IIb/III is PFS. Secondary endpoints of Phase IIa include pharmacokinetic ("**PK**") portfolio, immunogenicity, biomarkers and preliminary efficacy. Secondary endpoints of Phase IIb/III include ORR, disease control rate ("**DCR**"), OS, adverse events ("**AE**") and serious adverse events ("**SAE**"), and ADA.

Trial Status. We plan to initiate the Phase II clinical trial in the second quarter of 2024.

Phase I clinical trial in patients with advanced malignant tumors

Trial Design. This trial was a Phase I, open-label study designed to characterize the safety, tolerability, and preliminary effectiveness of IAP0971 in patients with advanced malignant tumors. This trial was conducted in China according to a protocol approved by both the NMPA and the FDA. This study includes two phases: the dose escalation, followed by the dose extension with reference to the MTD dose achieved from the dose escalation study.

As of the cut-off date (June 29, 2023), a total of 18 patients have been enrolled. The dose escalation study was initiated with 0.5μg/kg, 5μg/kg and 20μg/kg, and switched to 3+3 scheme starting from 60μg/kg, and then 120μg/kg and 200μg/kg every-other-week ("**Q2W**") subcutaneously. The primary objective of Phase I trial was to determine the MTD, DLT, and the incidence and frequency of AEs and SAEs. The secondary objectives included assessing PK portfolio, and immunogenicity of IAP0971.

Trial Status. We completed the Phase I clinical trial of IAP0971 in July 2023.

Safety Profile. As of the cut-off date (June 29, 2023), TRAEs were observed in 12 out of 15 assessable patients, accounting for a rate of 80.0%. The majority of these adverse events were classified as Grade 1-2, indicating mild to moderate severity. Grade 3-4 TRAEs were reported in seven patients, representing 46.7% of the cohort. These included lymphocytopenia (seven patients), fever (one patient), hyperbilirubinemia (one patient), intestinal infection (one patient), and amylase increased (one patient). For all the lymphocytopenia patients, they recovered after a period of observation without any medicine treatment. Furthermore, no DLTs were observed, and the MTD was not reached.

TRAEs occurring in ≥10% of patients or ≥ Grade 3 TRAEs

	All patients (N=15)	
	All grades, n (%)	≥Grade 3, n (%)
Any TRAE	12(80)	7(46.7)
TRAE in ≥10% of patients by preferred term and ≥ Grade 3 TRAEs		
Infusion related reaction	10(66.7)	0
Lymphocytopenia	7(46.7)	7(46.7)
Leukocytopenia	5(33.3)	0
Anaemia	5(33.3)	0
Fever	5(33.3)	1(6.6)
Thrombocytopenia	4(26.6)	0
Elevated AST	3(20)	0
Elevated ALT	3(20)	0
Hypoalbuminemia	3(20)	0
CRS	2(13.3)	0
Neutropenia	2(13.3)	0
Hyperbilirubinemia	2(13.3)	1(6.6)
Elevated γ-GT	2(13.3)	0
Cough	2(13.3)	0
Elevated amylase	1(6.6)	1(6.6)
Intestinal infection	1(6.6)	1(6.6)

Abbreviations: TRAE = treatment-related adverse event; CRS = cytokine release syndrome.

Note: Data cut-off: June 29, 2023; AEs graded according to NCI CTCAEv.5.0.

Source: Company data

Efficacy Profile. As of June 29, 2023, a total of 15 subjects were assessed in the study, of which eleven subjects were considered evaluable for efficacy analysis. Evaluable subjects were defined as those who had undergone at least one tumor assessment after baseline. Preliminary efficacy findings demonstrated that out of the eleven evaluable subjects, four heavily pretreated patients who failed and became resistant to all previous chemotherapies/immunotherapies (one with colorectal cancer ("**CRC**"), one with cervical cancer, and two with NSCLC) achieved stable disease. This resulted in a DCR of 36.4%.

The table below provides a detailed overview of the previous treatment profiles for patients who achieved a best response of SD.

Group	Patient	Previous Treatment	Efficacy
20μg/kg	CRC with combined lung metastases, bone metastases and pleural effusion	Resistant to oxaliplatin and capecitabine in the front-line treatment, followed by irinotecan + raltitrexed + bevacizumab + cetuximab	Achieved SD in the first evaluation after two cycles of IAP0971 administration
120μg/kg	Cervical cancer with combined pelvic metastases	Resistant to radiotherapy combined with nedaplatin chemotherapy, paclitaxel liposome combined with carboplatin chemotherapy, paclitaxel liposome combined with sintilizumab monoclonal antibody therapy, docetaxel combined with sintilizumab, docetaxel combined with cisplatin chemotherapy, oral apatinib combined with capecitabine treatment, and tireprizu combined with anlotinib and tegio capsules	Achieved SD in the first evaluation after two cycles of IAP0971 administration
120μg/kg	NSCLC with lung, adrenal gland and other (retroperitoneal/ right abdominal sulcus) metastases	Resistant to pemetrexed + lobaplatin + endostar chemotherapy; pemetrexed + nedaplatin + endostar chemotherapy; paclitaxel liposome + gemcitabine + endostar chemotherapy; camrelizumab + paclitaxel liposome + gemcitabine; camrelizumab + docetaxel + gemcitabine; camrelizumab + albumin paclitaxel; camrelizumab + gemcitabine; camrelizumab combined with erlotinib; sintilizumab + irinotecan + cisplatin + bevacizumab; sintilizumab + irinotecan + bevacizumab + carboplatin; the combination of sintilizumab + bevacizumab and vinorelbine	Achieved SD in the first evaluation after two cycles of IAP0971 administration

Group	Patient	Previous Treatment	Efficacy
200μg/kg	Adenocarcinoma of right lung with lung and other (pleura, pleural effusion) metastases	Resistant to intrathoracic infusion of bevacizumab; pemetrexed combined with cisplatin and bevacizumab; gefitinib combined with bevacizumab, and then changed to albumin-paclitaxel combined with nedaplatin chemotherapy; erlotinib and then osimertinib	Achieved SD at first efficacy evaluation after two cycles of IAP0971 administration

Abbreviations: CRC = colorectal cancer; NSCLC = non-small cell lung cancer; SD = stable disease.

Note:

Data cut off on June 29, 2023.

Source: Company data

Conclusion. Based on the data from this clinical trial, IAP0971 has demonstrated a favorable profile in terms of both safety and preliminary efficacy in heavily pretreated patients with advanced malignant tumors. Our safety data also shows IAP0971 can be given safely in subjects up to 200ug/kg Q2W subcutaneously.

Phase I clinical trial in NMIBC patients who have failed BCG treatment, and are considered unsuitable for radical cystectomy, or choose not to undergo the procedure

Trial Design. This is a single-arm, open label, multicenter Phase I clinical trial to evaluate the safety and efficacy of IAP0971 monotherapy or in combination with BCG therapy. This clinical trial will be conducted in China according to the protocol approved by both the NMPA and the FDA. Phase Ia of this study to evaluate IAP0971 as a monotherapy adopts the classic "3+3" dose-escalation design, with three to six assessable NMIBC patients who are non-responsive to or relapsed on BCG treatment included in each group. Phase Ib of this study adopts a similar design to evaluate IAP0971 in combination with BCG therapy. Administration method in both stages is intravesical instillation.

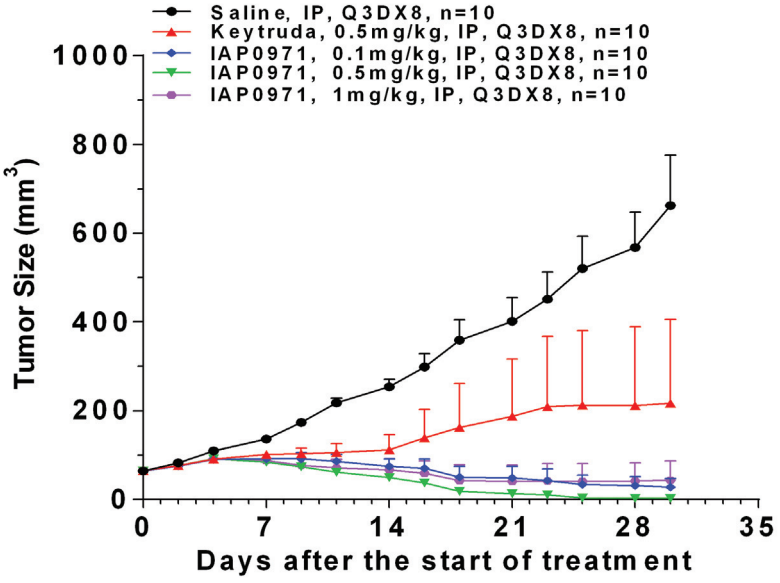
Primary endpoints of this study are the occurrence of AEs and DLT. Secondary endpoints include CR rate, DoR, disease free survival, PFS, time to cystectomy, and radical cystectomy rate.

Trial Status. We obtained the IND approval from the NMPA and the FDA in May 2023 and August 2023, respectively, with the first patient being dosed in China in March 2024.

Summary of preclinical study

In pharmacokinetic analysis, IAP0971 showed a half-life of 15.7 hours, which is approximately 15-fold longer than that of recombinant IL-15, and approximately 2-fold longer than that of an IL-15-Fc fusion protein. In addition, IAP0971 was also well tolerated up to 1.0 mg/kg when subcutaneously administered in the mouse model. In the repeated-dose toxicity study in cynomolgus monkeys, IAP0971 showed a favorable safety profile even at 1.2 mg/kg, around 40-fold higher than an IL-15-Fc fusion protein.

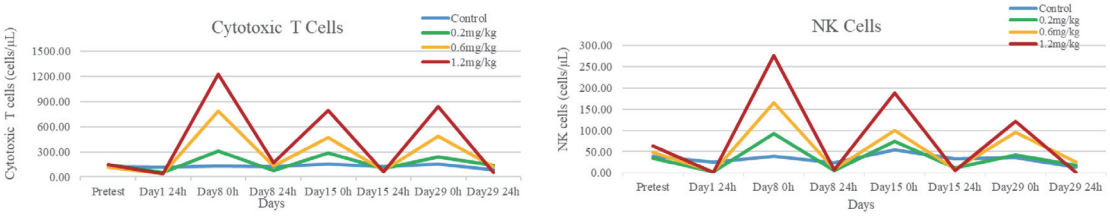
Our preclinical study showed that IAP0971 was well tolerated and exhibited excellent TGI in MC38-hPD-L1 C57BL/6 hPD1 mice model. IAP0971 was shown to be more effective in inhibiting tumor growth than Keytruda in the murine model. When intraperitoneally injected with 0.1mg/kg, 0.5mg/kg and 1mg/kg of IAP0971 every three days ("**Q3D**"), MC38-hPD-L1 C57BL/6 hPD1 mice showed significantly improved TGI comparing to 0.5 mg/kg Keytruda alone intraperitoneally injected Q3D. Data showed that at 0.1 mg/kg, 0.5 mg/kg and 1 mg/kg, IAP0971 demonstrated remarkable TGI rates of 106.13%, 110.47%, and 103.56%, respectively. Specifically, in the 0.1 mg/kg group, eight animals treated with IAP0971 achieved complete tumor regression, in the 0.5 mg/kg group, nine animals experienced complete response after treatment with IAP0971, and in the 1 mg/kg group, nine animals achieved complete tumor regression. The IAP0971 0.5 mg/kg group displayed superior tumor inhibition compared to the Keytruda 0.5 mg/kg group (110.47% when treated with 0.5mg/kg of IAP0971 vs. 75% when treated with 0.5mg/kg of Keytruda) and complete tumor regression rate (90% when treated with 0.5mg/kg of IAP0971 vs. 50% when treated with 0.5mg/kg of Keytruda).



Source: Company data

In another preclinical study conducted in cynomolgus monkeys, we specifically investigated the impact of IAP0971 on the proliferative activity of immune cells. The collected data revealed the effectiveness of IAP0971 in promoting the proliferation of CD8+ T lymphocytes and NK cells at various doses. Elevated levels of lymphocytes were sustained even seven days after the initial dose.

Proliferation of Cytotoxic T Cells and NK Cells after IAP0971 Dosing



Source: Company data

Conclusion. Based on the preclinical studies, IAP0971 demonstrates not only the biological activity of targeting a single pathway but also the advantageous dual-target synergistic effect. It not only activates T-cells but also stimulates NK-cell activation, enabling effective tumor cell growth inhibition.

Clinical Development Plan

We are executing a comprehensive clinical trial development plan in China and the U.S. targeting an array of cancer indications for our IAP0971. Our clinical development plan for IAP0971 involves first targeting an indication of significant unmet medical needs so that to quickly launch it on the China market, and then further expanding its potential application to major indications and other treatment areas to fully explore its potential.

Fast-to-Market Strategy

- 2L/3L BCG-unresponsive high risk NMIBC

According to Frost & Sullivan, globally, there were approximately 118.9 thousand new cases of 2L BCG-unresponsive high risk NMIBC in 2022, and the number is projected to reach 155.5 thousand in 2030. The number of new cases of 3L BCG-unresponsive high risk NMIBC was 64.2 thousand in 2022, and is anticipated to grow to 84.0 thousand in 2030. In China, there were approximately 25.7 thousand new cases of 2L BCG-unresponsive high risk NMIBC in 2022, and the number is projected to reach 34.1 thousand in 2030. The number of new cases of 3L BCG-unresponsive high risk NMIBC was 13.9 thousand in 2022, and is anticipated to grow to 18.4 thousand in 2030. The five-year survival rate of BCG-unresponsive high risk NMIBC is 72%.

Intravesical instillations with BCG have served as an established adjuvant therapy for NMIBC. Currently, the administration of intravesical BCG instillations subsequent to transurethral resection of the bladder tumor represents a crucial component of standard care for patients diagnosed with high-risk NMIBC. Although BCG is more effective than chemotherapy in patients with high-risk NMIBC, non-responsiveness to BCG treatment is observed in over 40% of this patient population, and 15% of them will progress to a muscle-invasive disease.

Immunotherapy has long been recognized as a viable approach in the management of NMIBC. According to Frost & Sullivan, anti-PD-1 antibody is considered a promising therapy for the treatment of 2L/3L BCG-unresponsive high risk NMIBC, with the complete response rate ("**CRR**") being approximately 41%. In January 2020, Keytruda monotherapy was approved by the FDA for BCG-unresponsive carcinoma *in situ* ("**CIS**") patients with high-risk NMIBC. In addition, N-803, an IL-15/IL-15Rα complex fused to an IgG1 Fc, in combination with intravesical BCG was examined and also achieved encouraging clinical results as a potential treatment for BCG-unresponsive NMIBC. Although the FDA did not approve the BLA of N-803 according to its complete response letter on May 9, 2023, the deficiencies are not safety or efficacy in nature but relate to third-party contract manufacturing organizations and CMC issues. In addition, in October 2023, the FDA accepted the resubmitted BLA of N-803 and set a new Prescription Drug User Fee Act date for April next year.

Given that Keytruda was approved by the FDA and N-803 combined with BCG has demonstrated its potential in treating BCG-unresponsive high risk NMIBC patients, and based on the fact that IAP0971 combines the targets from both drugs and accordingly is expected to have the full potential of these two drugs, we plan to conduct a Phase I trial in 2L/3L BCG-unresponsive NMIBC in China. We have obtained the IND approval for conducting Phase I and Phase II clinical trials from the NMPA and the FDA in May 2023 and August 2023, respectively, enrolled the first patient of the Phase I clinical study in China in March 2024, and expect to start a pivotal Phase II trial in the fourth quarter of 2024.

Major Indications

- 1L/2L Advanced NSCLC

We are currently assessing the potential of IAP0971 as a monotherapy for highly prevalent cancer types. In recent years, anti-PD-1 antibodies have become the standard of care for various tumor types. It can be expected that there will be urgent medical needs for effective treatments targeting PD-1/PD-L1 R/R tumors. Given the demonstrated efficacy of PD-1 and IL-15 combination therapy following PD-1 immunotherapy across different tumor types, we anticipate that IAP0971, as a PD-1/IL-15 immunocytokine, holds clinical potential for treating cancer types with significant unmet medical needs, particularly PD-1/PD-L1 R/R tumors.

According to Frost & Sullivan, globally, there were approximately 1,329.6 thousand new cases of 1L advanced NSCLC in 2022, and the number is projected to reach 1,709.3 thousand in 2030. The number of new cases of 2L advanced NSCLC was 930.7 thousand in 2022, and is anticipated to grow to 1,196.5 thousand in 2030. In China, there were approximately 561.7

thousand new cases of 1L advanced NSCLC in 2022, and the number is projected to reach 733.6 thousand in 2030. The number of new cases of 2L advanced NSCLC was 393.2 thousand in 2022, and is anticipated to grow to 513.5 thousand in 2030. See "Industry Overview — Immuno-Oncology Drugs Overview — Major Indications for Immuno-Oncology Therapies — NSCLC" in this document for further information regarding the patient population for 1L advanced non-squamous NSCLC and 2L advanced squamous NSCLC. For advanced NSCLC, the five-year survival rate can be extremely low, at approximately 9%. Anti-PD-1 antibody is considered a promising therapy for the treatment of 1L/2L NSCLC. For 1L advanced NSCLC, the ORR is 27% in tumors with as low as 1% expressing PD-1, i.e. a tumor proportion score ("**TPS**") ≥1%. For 2L advanced NSCLC, the ORR is 18% in PD-1 positive tumors with TPS ≥1%.

In treating NSCLC, we plan to explore both monotherapy and combination therapy, and investigate IAP0971 through subcutaneous administration. In the context of monotherapy, our focus is on investigating the potential of IAP0971 as a treatment for 2L advanced NSCLC. We plan to conduct a Phase II clinical trial of IAP0971 for locally advanced unresectable or metastatic NSCLC patients as second-line treatment, and enroll the first NSCLC patient in the second quarter of 2024.

In addition, we plan to explore IAP0971 in combination with pemetrexed and platinum in 1L non-squamous NSCLC as first-line treatment. The efficacy and safety profile demonstrated in our Phase I clinical trial of IAP0971, along with encouraging outcomes in trials combining anti-PD-1/PD-L1 antibodies with chemotherapy, support our approach. We plan to submit an IND application and after receiving the approval, enroll the first patient in a Phase II clinical trial of IAP0971 in the third quarter of 2024.

Indication Expansion to Anti-Viral Infection

- Chronic HBV Infection

In addition to exploring IAP0971's potential in oncology, we plan to examine IAP0971 as an immunotherapy for the treatment of viral infectious diseases, especially hepatitis B, which is one of the most prevalent infectious diseases in China, according to the National Health Commission. According to Frost & Sullivan, there were approximately 8,978.3 thousand new cases of chronic HBV infection globally in 2022, and the number is projected to reach 21,503.2 thousand in 2030. In 2022, there were approximately 2,182.3 thousand new cases of chronic HBV infection in China, and the number is projected to reach 4,993.0 thousand in 2030. The five-year survival rate of chronic HBV infection is approximately 89%.

In chronic viral hepatitis, upregulation of PD-1 and CTLA-4 is associated with T-cell exhaustion and persistent viral infection, favoring the chronicity of viral disease but limiting immunopathogenesis. Therefore, ICIs, including anti-PD-1 inhibitor, can potentially improve T-cell function by blocking PD-1-mediated signaling, a pathway that is confirmed to play an important role in inducing T-cell exhaustion. According to Frost & Sullivan, currently, there is no approved PD-(L)1 inhibitors indicated for HBV. However, ASC22, a PD-L1 antibody, has

shown potential for curing CHB patients. Data from Phase IIa clinical trials showed a dose-dependent decline in hepatitis B surface antigen after a single dose of ASC22. In addition, an exploratory Phase I clinical trial of N-803 for HIV infection has shown that N-803 was associated with proliferation and/or activation of CD4+ and CD8+ T cells and natural killer cells. Therefore, IAP0971 can potentially alleviate the T-cell exhaustion through the activation of both innate and adaptive immunity in patients with chronic HBV infection. We plan to submit an IND application for a Phase I clinical trial for chronic HBV infection in the third quarter of 2024 to explore IAP0971's anti-viral infection potential.

Global Strategy

We are carrying out a global strategy in the clinical development of IAP0971. In the U.S., we have obtained an IND approval for investigating IAP0971 as a monotherapy in advanced malignant tumors in December 2021. Because the Phase I and Phase II clinical trial designs approved by the NMPA and the FDA are the same including the site (located in China) and PI of the clinical trial, we plan to leverage the clinical data from the Phase I trial in China, carefully decide our clinical development plan in the U.S., communicate with the FDA regarding the Phase II clinical trial design, and upon reaching an agreement with the FDA regarding the trial design, initiate Phase II clinical trials for selected tumor types in the U.S. according to the FDA approved clinical trial design either by ourselves or through international collaboration. Alternatively, depending on the specific clinical stage and therapeutic regimen we carefully decide upon in the future, we will submit a new IND application to the FDA when new IND approval is required. Considering the costs, we decided to proceed with clinical trials in China first. As of the Latest Practicable Date, we had not commenced the clinical trials in the U.S. and had not planed to commence the trials in the U.S. within the coming six months.

Although the FDA has issued the IND approval and accepted that Phase I and Phase II clinical trials of IAP0971 can be conducted in China, we cannot guarantee that the FDA will accept our clinical results generated in China to support future clinical trials in the U.S., and we may face difficulties and incur additional costs thereof. For details, see "Risk Factors — Risks Relating to Government Regulations — We Primarily Conduct Clinical Trials for Our Drug Candidates in China, While FDA or Comparable Foreign Regulatory Authorities May Not Accept Data From Such Trials" in this document.

Licenses, Rights and Obligations

IAP0971 was developed by us, and we maintain the global rights to develop and commercialize this drug candidate.

Material Communications With Competent Authorities

The material communications with the relevant competent authorities on all ongoing and completed clinical trials in respect of the Core Product IAP0971 are as follows:

- In December 2021, we received the IND approval from the FDA for conducting Phase I and Phase II clinical trials of IAP0971 in patients with advanced malignant tumors.

- In January 2022, we received the IND approval from the NMPA for conducting Phase I and Phase II clinical trials of IAP0971 in patients with advanced malignant tumors.

- In May 2023, we received the IND approval of IAP0971 from the NMPA to conduct Phase I and Phase II clinical trials using IAP0971 monotherapy or in combination with BCG for high risk BCG-unresponsive NMIBC.

- In August 2023, we received the IND approval of IAP0971 from the FDA to conduct Phase I and Phase II clinical trials using IAP0971 monotherapy or in combination with BCG for high risk BCG-unresponsive NMIBC.

- In September 2023, we conducted an interview with a senior examiner of the NMPA with the attendance of professional parties, which reconfirmed, amongst others, that the Phase I clinical trial of IAP0971 has been completed, and based on the safety and efficacy data from the Phase I clinical trial, that the NMPA had no objection for us to commence a planned Phase II clinical trial of IAP0971 as a monotherapy for locally advanced unresectable or metastatic NSCLC.

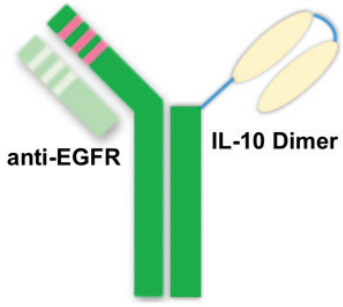
- In December 2023, we conducted a phone interview with the Director of Nanjing Inspection Branch, Jiangsu Provincial Medical Products Administration, which is a provincial branch regulated by the NMPA, with the participation of professional parties (the "**Regulatory Phone Interview**"). During the Regulatory Phone Interview, the Director confirmed that approval of drugs is managed by the approval number, which corresponds to the registration certificate of a drug, and the approval will encompass any different indications or combination therapy approved for marketing. In addition, if there are new indications or combination therapy for a marketed drug, the company can also make a supplemental application, but the company will not receive a new approval number for the same drug. Therefore, the monotherapy and combination therapy of the same drug for different indications, once approved by the NMPA, will be regulated under the same drug certificate in China.

We have not received any concerns or objections from the NMPA or the FDA related to receiving IND approvals, conducting the Phase II clinical trial, or executing our clinical development plans as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IAP0971 SUCCESSFULLY

Core Product: IAE0972 (EGFR/IL-10 antibody-cytokine fusion protein)

IAE0972 is a clinical stage, dual-moiety, anti- EGFR antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation. It is designed to bind to EGFR and trigger blockage of downstream signaling pathways that contribute to cell death suppression and promote cell proliferation, and deliver IL-10 to activate CD8+ T cells in the TME. The diagram below illustrates the structure of IAE0972:



Source: Company data

We implement a global registration strategy for IAE0972. We received IND approvals for conducting Phase I and Phase II clinical trials of IAE0972 for advanced solid tumors from the NMPA and the FDA in January 2022 and December 2021, respectively, and commenced the Phase I clinical trial in June 2022. In July 2023, we completed the Phase I clinical trial of IAE0972 in patients with advanced solid tumors in China. We have initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first HNSCC patient and the first CRC patient in July 2023 and December 2023, respectively. In addition, we received the IND approval from the NMPA for conducting Phase II and Phase III clinical trials of IAE0972 in combination with lenvatinib in patients with locally advanced or metastatic HCC as first-line treatment in November 2023. We expect to commence a Phase II clinical trial for HCC in the second quarter of 2024.

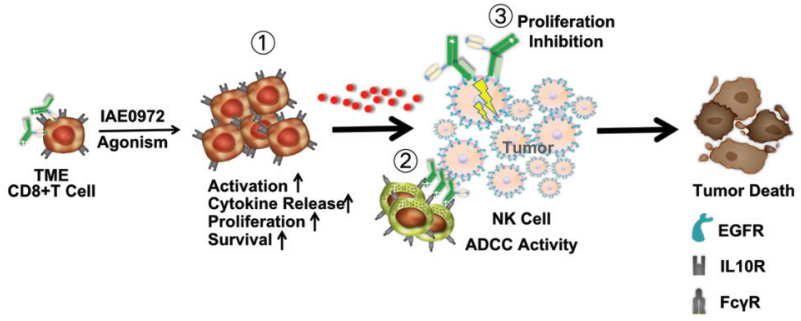
Mechanism of Action

IL-10 is one group of cytokines mainly produced by activated macrophages and certain T lymphocytes. It is a noncovalent homodimer in its natural form. IL-10 interacts with its receptor IL-10R, which is expressed on the surface of most hematopoietic cells, including T cells, B cells, and macrophages. Upon binding, IL-10 will be able to activate tumor-infiltrating memory-killing CD8+ T cells and even reactivate terminally exhausted T cells, and potentially NK cells and thereby convert the immunosuppressive TME into pro-inflammatory TME. In addition, IL-10 has strong antitumor activities and primarily acts on the TME, which reduces systemic cytotoxicity and is considered relatively safe among cytokines, producing immune cell activation and significant alterations in host physiology. It is because that naïve T cells in

peripheral have very low IL-10R expression, while antigen-specific tumor infiltrating and memory T cells in the TME have high IL-10R. Therefore, treatment strategies involving IL-10 may represent a potential solution for patients who suffer from primary or acquired drug resistance to immunotherapies, especially acquired drug resistance to immune checkpoint inhibitors caused by T cell exhaustion.

EGFR is a receptor tyrosine kinase involved in the proliferation and survival of cancer cells, and it is overexpressed in many cancer types including head and neck, breast, lung, colorectal, prostate, kidney, pancreas, ovary, brain and bladder cancer. The EGFR is activated via extracellular ligand binding, inducing phosphorylation of specific residues of the EGFR. This in turn will activate several downstream signaling pathways and finally promote or regulate cell proliferation, differentiation, invasion, angiogenesis and avoidance of apoptosis.

IAE0972 is an immunocytokine consisting of an anti-EGFR antibody fragment and an IL-10 homodimer. It adopts an asymmetric structure, which consists of a monovalent anti-EGFR antibody fragment and a homodimer of IL-10. Such a design is expected to reduce the binding activity of anti-EGFR antibody on EGFR-low expression normal cells while preserving the biological activity on EGFR-high expression tumor cells and thus reduce EGFR-related skin toxicities. The anti-EGFR antibody fragment targets EGFR and inhibits tumor growth through blockage of the EGFR signaling pathway. It also serves as a tumor-associated antigen for tumor-targeted delivery of IL-10 to EGFR-positive tumor cells. As such, IAE0972 activates the CD8+ T cells and potentially NK cells and direct them to the targeted local tumor lesion and reduces the skin toxicity commonly observed for IL-10-based treatment. By linking to the IL-10 homodimer, the antibody fragment portion also extends the half-life of IL-10 and therefore prolongs the therapeutic window of IAE0972.



Source: Company data

Similarities and Differences of the Antibody Moiety of IAE0972 Compared to Marketed Anti-EGFR Antibodies or Those in Clinical Trials

IAE0972, as an antibody-cytokine fusion protein, combines an anti-EGFR antibody with an IL-10 homodimer. Compared to the marketed anti-EGFR antibodies or those in clinical trials, IAE0972 shares a similar mechanism of action in which the anti-EGFR antibody targets and blocks the EGFR protein on tumor cells, thereby inhibiting their growth. However, IAE0972 differs in that its anti-EGFR antibody is monovalent, aimed at reducing the risk of skin toxicity. Structurally, it forms heterodimers using a "knobs-into-holes" structure, while current anti-EGFR antibodies, whether marketed or in clinical trials, are homodimers. Additionally, IL-10 within IAE0972 functions as an EGFR-specific T cell activator, enhancing its antitumor efficacy. These distinctions highlight the unique attributes of IAE0972, as outlined in the table below.

A Comparison of the Antibody Moiety of IAE0972 with Marketed Anti-EGFR Antibodies and Selected Ones in Clinical Trials

Categories	IAE0972	Marketed Anti-EGFR Antibodies or Selected Ones in Clinical Trials			
	Anti-EGFR Antibody Moiety of IAE0972	cetuximab	matuzumab	panitumumab	necitumumab
Similarities					
MoA of the Antibody or Antibody Moiety	Binds to the EGFR protein on the surface of tumor cells to block tumor cell growth signals; targets the tumor microenvironment				
Subtype Class	IgG1	IgG1	IgG1	IgG2	IgG1
Differences					
Antibodies' Valency	Monovalent to reduce the toxicity to skin	Bivalent	Bivalent	Bivalent	Bivalent
Structure	Heterodimer. The heavy chains have "knobs-into-holes" amino acid changes.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.	Homodimer. No "knobs-into-holes" mutations.
Antitumor Mechanism	Simultaneously binds to EGFR and IL-10 to activate T cells in the TME	No TME-specific T cell activation	No TME-specific T cell activation	No TME-specific T cell activation	No TME-specific T cell activation
In Vivo Effect	In a head-to-head in vivo study in the C57BL/6 mouse allograft tumor model, IAE0972 demonstrated significantly improved antitumor effect.	No head-to-head comparison available			

Market Opportunities and Competition

Based on the preliminary efficacy data obtained from our Phase I clinical trial, we plan to conduct a Phase II clinical trial of IAE0972 for CRC. Considering the mechanism of action and clinical data for EGFR targeted therapies from other researchers, we also plan to explore IAE0972's potential in the treatment of HNSCC, HCC and NSCLC.

HNSCC

Head and neck cancer is a group of cancers that arises in the mouth, nose, throat, larynx, sinuses, or salivary glands. Head and neck squamous cell carcinoma ("**HNSCC**") is the most common subtype that accounts for more than 90% of head and neck cancers. According to Frost & Sullivan, the global market of head and neck cancer drugs increased from US$2.9 billion to US$4.6 billion with a CAGR of 12.3% from 2018 to 2022, and is projected to reach US$6.4 billion in 2026 and US$8.7 billion in 2030. The China market of head and neck cancer drugs increased from US$0.3 billion to US$0.6 billion with a CAGR of 18.6% from 2018 to 2022, and is projected to reach US$1.2 billion in 2026 and US$1.8 billion in 2030 with a CAGR of 19.2% and 11.1% from 2022 to 2026 and from 2026 to 2030, respectively.

While PD-1-targeted immunotherapy has been established as the preferred first-line treatment for metastatic HNSCC, surpassing the efficacy of chemotherapy combined with cetuximab, a notable proportion of patients do not experience benefits from this approach. For example, Keytruda, when administered in conjunction with chemotherapy, demonstrates a modest ORR of only 36% in patients exhibiting positive PD-L1 expression (Combined Positive Score, CPS $\geq$ 1). Additionally, if patients fail to respond to first-line therapy, there is a paucity of effective follow-up treatment options. Specifically, although PD-1 inhibitors are recommended as second-line treatment, their efficacy in managing HNSCC patients with disease progression remains unsatisfactory, yielding an ORR ranging from 13.3% to 16%. Consequently, there is an urgent demand for novel treatment alternatives that can enhance the response rate of PD-1-targeted immunotherapy and achieve more efficacious eradication of tumors. For further details, see "Industry Overview — Immuno-Oncology Drugs Overview — Major Indications for Immuno-Oncology Therapies — HNSCC" in this document.

CRC

See "— Drug Candidates — Core Product: IAE0972 (EGFR/IL-10 antibody-cytokine fusion protein) — Market Opportunities and Competition — CRC" in this section for information related to market opportunities.

HCC

Liver cancer is the growth and spread of unhealthy cells in the liver. Hepatocellular carcinoma ("**HCC**") is the most common type of primary liver cancer (~90%), and is the most common cause of death in people with cirrhosis. According to Frost & Sullivan, the global market for HCC drugs increased from US$1.7 billion in 2018 to US$3.1 billion in 2022,

representing a CAGR of 16.5% during this period. Projections suggest this figure will reach US$6.6 billion in 2026 and US$11.2 billion in 2030, with anticipated CAGRs of 21.0% from 2022 to 2026 and 14.0% from 2026 to 2030, respectively. Similarly, the Chinese market for HCC drugs rose from US$0.7 billion in 2018 to US$1.5 billion in 2022, demonstrating a CAGR of 21.7% from 2018 to 2022. It is forecasted to reach US$3.7 billion in 2026 and US$6.2 billion in 2030, with projected CAGRs of 24.4% from 2022 to 2026 and 14.2% from 2026 to 2030, respectively.

Therapeutic options for HCC are generally determined based on disease staging. For late-stage HCC, systemic therapies are primarily recommended for first- and second-line treatments, two major classes of which are small molecule targeted drugs, such as NEXAVAR® (sorafenib), LENVIMA® (lenvatinib) and immune checkpoint inhibitors (e.g., PD-1/PD-L1 inhibitors). The corresponding combination therapies of targeted drugs or immune checkpoint inhibitors are also commonly used in first- and second-line treatments.

Due to the limited clinical outcomes associated with small molecule targeted drugs, PD-1/PD-L1 inhibitors have been introduced in the first- and second-line settings to improve treatment outcomes for HCC patients in recent years. However, current immuno-oncology therapy regimens still fail to yield material progression-free and overall survival benefits. For example, although the combination of a PD-1/PD-L1 inhibitor and anti-VEGF therapy, such as atezolizumab or sintilimab plus bevacizumab, has demonstrated certain efficacy (an overall mPFS of around 4 months), there is still room for improvement, indicating a need for more effective strategies.

NSCLC

See "— Drug Candidates — Core Product: IAP0971 (PD-1/IL-15 antibody-cytokine fusion protein) — Market Opportunities and Competition — NSCLC" in this section for information related to market opportunities.

Competitive Landscape

Currently, there are no approved IL-10 based immunotherapies indicated for the treatment of cancer according to Frost & Sullivan. Both globally and in China, three IL-10 based immunotherapies are currently under clinical development with two of them from us, i.e. IAE0972 and IBB0979. As of the Latest Practicable Date, our IAE0972 was in Phase II clinical stage and IBB0979 was in Phase I/II clinical stage, and they were the most clinically advanced IL-10 based immunocytokine in China.

Competitive Advantages

IAE0972 is another immunocytokine developed from our AIC™ Platform. It is the first anti-EGFR antibody/IL-10 immunocytokine that received IND approvals from both the NMPA and FDA. Through the distinct mechanism of simultaneously binding to EGFR and receptor of IL-10, IAE0972 activates antigen-specific CD8+ T cells in the TME, leading to a revival of tumor-killing activity in exhausted T cells.

Advantages in terms of molecular design

IAE0972 effectively targets both EGFR and the IL-10 receptor, facilitating the activation of CD8+ T cells within the TME. The anti-EGFR antibody component of IAE0972 specifically directs IL-10 to tumor tissues, mitigating the systemic toxicity of IL-10. This targeted approach enables a significantly higher safe dosage of IAE0972, approximately 300 times greater than the clinical dose of PEGylated IL-10. By binding to IL-10R on EGFR-specific CD8+ T cells, IL-10 promotes their expansion and activation, leading to the efficient elimination of EGFR-high expressing tumor cells and overcoming drug resistance commonly associated with EGFR mAbs.

- **Asymmetric structure design**. The monovalent design of IAE0972's anti-EGFR antibody component not only targets IL-10 specifically to tumor tissues but also reduces the skin toxicity associated with the anti-EGFR antibody. As a result, it significantly expands the therapeutic window of the drug.

  To address heavy chain mismatches, IAE0972 adopts an asymmetric heterodimeric structure in its Fc region, employing a knobs-into-holes structural design. This unique design not only enhances the stability of the drug but also ensures its efficacy.

- **Cytokine structure design**. The latest research indicates that IL-10 serves as a specific activator for antigen-activated CD8+ tumor-infiltrating lymphocytes in the TME. Due to the minimal expression of IL-10R in naïve T cells in peripheral blood, this specific activation is confined to the TME, necessitating the fusion of antibodies targeting tumor-related antigens with IL-10 to target IL-10 specifically to the TME. The IL-10 payload of IAE0972 naturally adopts a homodimeric structure, which provides enhanced immune cell activation activity and favorable CMC druggability. This characteristic makes it an ideal candidate for drug development purposes.

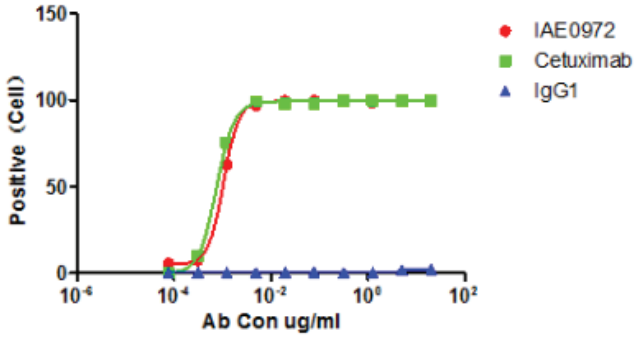
- **Synergistic Effect between anti-EGFR antibody and IL-10.** The EGFR protein is highly expressed in various tumor cells. Selecting anti-EGFR antibodies and fusing them with IL-10 can enrich IL-10 in TME of various tumors through anti-EGFR antibodies, potentially expanding the indications of this drug candidate. The anti-EGFR antibody moiety of IAE0972 is a chimeric antibody. It binds to antigen-specific CD8+ T lymphocytes expressing IL-10 receptors, promoting their proliferation and activation, thereby enhancing the safety and efficacy profile of the

drug. The role of the anti-EGFR antibody moiety of IAE0972 includes: 1) Enriching cytokines in the TME using anti-EGFR antibodies; 2) IAE0972 can simultaneously bind specifically to tumor cells and T cells to inhibit EGFR overexpression.

We have validated functionalities of IAE0972 through multiple preclinical studies of binding to EGFR overexpressing tumor cell line, dual target binding assay, *in vitro* CD8+ T cell activation assay, *in vitro* ADCC assay, and *in vivo* antitumor efficacy assay.

In a preclinical study, we verified that the anti-EGFR antibody in IAE0972 exhibits the same tumor-targeting effect as the marketed antibody, cetuximab. In the study, IAE0972 and the EGFR-positive tumor cells A549 were co-incubated, and the binding ability of IAE0972 to A549 was detected using PE-F(ab')2 Goat anti-human IgG Fcγ antibody as the secondary antibody, with cetuximab serving as a positive control. Data demonstrated that the binding ability of IAE0972 to A549 is equivalent to that of cetuximab.

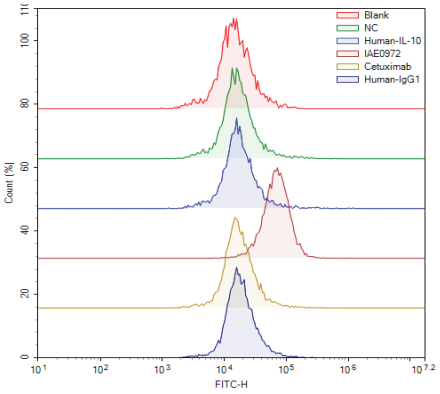
Binding of IAE0972 to A549



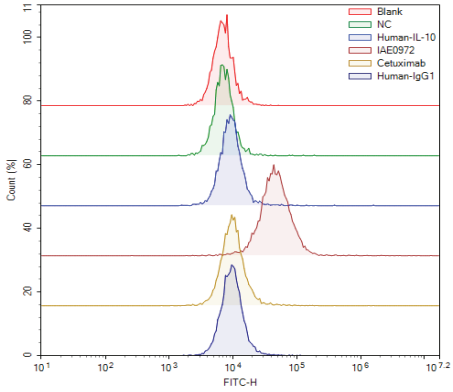
Source: Company data

In another preclinical study, we found that IAE0972 can simultaneously bind to EGFR and IL-10R receptors, whereas cetuximab cannot. Specifically, after incubating IAE0972 with IL-10RA protein, flow cytometry was used to detect the binding of IL-10 homodimer complex of IAE0972 to EGFR-positive MDA-MB-231 cells. Similarly, after binding IAE0972 to EGFR protein, flow cytometry was used to assess its binding to IL-10-Reporter-HEK-293 cells. Data demonstrated that IAE0972 can bind to both EGFR and IL-10R simultaneously, whereas the control cetuximab does not bind to IL-10R.

MDA-MB-231 cells



IL-10-Reporter-HEK-293 cells



Source: Company data

Further preclinical study results demonstrated that IAE0972 exhibited equimolar binding capacity to the IL-10R, similar to IL-10, and can selectively activate IL-10/IL-10R signaling. Moreover, IAE0972 also showed an excellent tumor inhibition effect in the C57BL/6 mouse allograft tumor model, superior to cetuximab. For details, see "— Drug Candidates — Core Product: IAE0972 (EGFR/IL-10 antibody-cytokine fusion protein) — Summary of Preclinical Data" in this section.

Favorable preclinical and clinical data

The IL-10 payload in IAE0972 enhances the killing effect of immune cells on EGFR-positive tumor cells. The inhibition rate of tumor growth in mice treated with IAE0972 reaches an impressive 83%, which is significantly better than that of an anti-EGFR mAb (20%). Moreover, the tolerated dose in cynomolgus monkeys reached 6mg/kg with no skin toxicity observed, surpassing that of the anti-EGFR mAb.

The potential toxic effects of IAE0972 were adequately exposed in multiple dosing trials, and the drug-related changes in cynomolgus monkeys in a repeat-dose toxicity study. We have focused on skin toxicity of the anti-EGFR antibody moiety and hematological toxicity of the IL-10 homodimer. The trial data showed that no drug-related skin toxicity was observed with IAE0972 at 6 mg/kg repeated dosing and 10 mg/kg single dosing, whereas literature data showed that cetuximab already exhibited mild skin toxicity at equivalent doses. This safety profile is in line with our structural design expectation that the anti-EGFR antibody of IAE0972 is monovalent, further reducing its skin toxicity and improving its safety of administration, while ensuring the targeting of the antibody.

When compared to an IL-10 cytokine product, IAE0972 demonstrates superior structural stability, enhanced targeting capabilities, extended half-life, and a significantly broader therapeutic window. In cynomolgus monkeys, IAE0972 exhibited a tolerated dose of 6mg/kg,

which is remarkably higher than the 15-20μg/kg dosage of the IL-10 cytokine product in clinical trials recorded in literatures. Consequently, the therapeutic window of IL-10 in IAE0972 has been expanded by 300-fold.

We evaluated IAE0972 in a Phase I clinical trial in patients with locally advanced or metastatic malignant tumors. In this trial, safety of IAE0972 was evaluated in pre-specified doses: 0.001 mg/kg, 0.01 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg and 2.5 mg/kg in cohorts of one to six patients each. As of the Latest Practicable Date, the Phase I clinical trial of IAE0972 have been completed in the 2.5mg/kg group, and favorable patient tolerability has been observed in all previous dose groups.

Potentially improved safety and efficacy than current anti-EGFR antibodies

EGFR is overexpressed in various tumors and correlates with the prognosis of malignant tumors, such as HNSCC, CRC and NSCLC. mAbs primarily target the extracellular domain of proteins, which are less likely to mutate, and thus the antitumor effect of the mAbs may less likely be affected by drug resistance due to intracellular amino acid mutations. However, their effectiveness and safety still pose challenges. The main antitumor mechanisms of the current anti-EGFR mAb, such as cetuximab, include blocking cell growth and inducing ADCC-mediated tumor cell killing, with skin toxicity observed at high doses. By reducing bivalent EGFR antibody into monovalent and fusing the antibody with IL-10, IAE0972 can effectively enrich IL-10 in the TME through anti-EGFR antibodies, further activating antigen-specific CD8+ T lymphocytes and significantly enhancing the safety and efficacy profile of this drug.

	IAE0972	**An anti-EGFR antibody**
Binding activity	similar	similar
***In vitro* tumor cell proliferation inhibition**	similar	similar
Dual EGFR/IL10R target binding activity	Yes	No
CD8+ T cell stimulation activity	Yes	No
Skin toxicity	Low	High
Tumor growth inhibition rate at 5mg/kg	83%	20%

Source: Company data

High and stable production rate

The company's asymmetric immunocytokine cell line technology has enabled the expression of IAE0972 to reach 2.9g/L, with a one-step affinity chromatography purity of about 85%. The final yield is about 50%, indicating excellent commercial scalability.

Despite the potential competitive advantages based on the mechanism of action, drug design, preclinical studies, and preliminary clinical data, the successful development of IAE0972 remains highly uncertain, primarily due to the absence of approved IL-10 based immunocytokines. Additionally, whether the anticipated clinical benefits of using anti-EGFR antibodies in the form of immunocytokines would materialize in targeted patients is still subject to further evaluation and validation in Phase II or later phases of clinical trials.

Summary of Clinical Trial Results

We have completed the Phase I clinical trial of IAE0972 in patients with advanced malignant tumors in China in July 2023. Based on the clinical results from the Phase I trial, upon communication with the principal investigator, we have initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first HNSCC patient and the first CRC patient in July 2023 and December 2023, respectively. As of the Latest Practicable Date, we have not received objection for entering a Phase II clinical trial from the NMPA.

Phase II clinical trial in patients with relapsed or metastatic HNSCC and metastatic CRC who have failed standard treatments

Trial Design. This study is a single arm, open label, multi-centered Phase II clinical study to evaluate the safety and efficacy of intravenous infusion of IAE0972 as a monotherapy in subjects with relapsed or metastatic HNSCC and metastatic CRC who have failed standard treatments. The study will be divided into two cohorts: cohort A will include subjects with recurrent or metastatic HNSCC who have failed standard treatments; cohort B will include subjects with metastatic CRC who have failed standard treatment. Subjects in the study will continue to receive intravenous infusion of IAE0972 until the occurrence of disease progression, initiation of new antitumor therapy, judgement by the investigator that continued participation is not appropriate, loss to follow-up, voluntary withdrawal, death, or study termination/suspension. Subjects will be assessed for tumors every six weeks (±7 days) during the study. AEs will be assessed in the study through clinical observation, vital signs monitoring, and laboratory tests of the subjects.

The primary endpoint of this study is ORR. Secondary endpoints include PFS, DCR, DoR, 6-month progression-free survival rate, 12-month progression-free survival rate and 12-month survival rate, AEs and SAEs, and major PK parameters and immunogenicity.

Trial Status. We have initiated this trial and enrolled the first HNSCC patient and the first CRC patient in July 2023 and December 2023, respectively.

Phase II clinical trial in patients with advanced HCC or advanced solid tumors by us

Trial Design. This is a Phase II, open-label, multicenter clinical study of IAE0972 in combination with lenvatinib in patients with advanced HCC or advanced solid tumors. The study will be conducted in two phases: IIa and IIb. Phase IIa will use the classic "3+3" design for dose escalation. Each group will include three to six subjects with locally advanced/metastatic solid tumors who have failed standard treatment, or have no standard treatment options, or for whom standard treatment is not applicable at this stage. The starting dose of IAE0972 will be 2.5mg/kg QW administered intravenously, and lenvatinib will be administered orally with either 12mg or 8mg, depending on the subject's weight. Escalation dose will be determined based on the safety and efficacy data obtained in this study. Each treatment cycle is defined as 3 weeks. Phase IIb will be commenced after obtaining RP2D from the Phase IIa study. We expect to enroll unsystematically treated subjects with locally advanced/metastatic HCC who are not candidates for surgical and/or localized therapy, or who have experienced disease progression after undergoing surgical and/or localized therapy. The subjects will continue to receive IAE0972 in combination with lenvatinib until the occurrence of any endpoint event.

The primary objective of the Phase IIa study includes safety, tolerability, DLT and/or RP2D. The secondary objective includes PK, immunogenicity and preliminary efficacy. The primary objective of the Phase IIb study includes preliminary efficacy. The secondary objective includes safety, tolerability and immunogenicity.

Trial Status. We obtained the IND approval from the NMPA to conduct this clinical trial in November 2023.

Phase I clinical trial in patients with advanced or metastatic solid tumors

Trial Design. This trial was a Phase I, open-label study of IAE0972 in patients with selected advanced or metastatic solid tumors. This trial was conducted in China according to a protocol approved by both the NMPA and the FDA. The Phase I stage of the clinical trial aims to characterize the safety, tolerability, PK, immunogenicity, and preliminary antitumor activity of IAE0972 in previously treated patients with advanced solid tumors. Each treatment cycle spanned 4 weeks, during which IAE0972 was administered intravenously (IV) on Days 1, 8, 15 and 22. Tumor assessments was performed every 8 weeks, just prior to dosing for Cycles 3, 5, 7 and so on. Patients who did not experience a DLT or any other unacceptable toxicity that necessitated permanent discontinuation of the investigational product were eligible to continue treatment. Treatment discontinuation could occur upon documented disease progression, initiation of alternative anti-cancer therapy, loss to follow-up, withdrawal of informed consent, death, or at the end of the study.

The DLT evaluation period, specifically, encompasses the 28 days following the IV administration of the first dose of IAE0972 (Cycle 1). IAE0972 was evaluated across pre-specified dose levels: 0.001 mg/kg, 0.01 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg and 2.5

mg/kg with each cohort consisting of 1 to 6 patients. Additionally, lower, intermediate, or higher dose levels could be explored. Subsequent to the last dose of IAE0972, each patient's overall survival ("**OS**") will be monitored, with assessments conducted at 12-week intervals.

The primary objectives include safety and tolerability. The secondary objectives include PK portfolio, and immunogenicity of IAE0972.

Trial Status. We completed this Phase I clinical trial of IAE0972 in July 2023.

Safety Profile. As of the cut-off date (June 29, 2023), a safety evaluation was conducted on a total of 14 subjects enrolled in the dose escalation phase of IAE0972. Most of the patients experienced Grade 1 or 2 TRAEs, only one (7.1%) experienced Grade 3 TRAE, which was apocleisis. No Grade 4-5 TRAEs occurred. No DLT occurred and MTD was not reached.

TRAEs occurring in ≥10% of patients or ≥ Grade 3 TRAEs

	All patients (N=14)	
	All grades, n (%)	**≥Grade 3, n (%)**
Any TRAE	14(100.0)	1(7.1)
TRAE in ≥10% of patients and ≥ Grade 3 TRAEs by preferred term		
Anaemia	6(42.9)	0
IL increased	6(42.9)	0
Fatigue	3(21.4)	0
Bilirubin increased	3(21.4)	0
Apocleisis	3(21.4)	1(7.1)
Hypoalbuminemia	2(14.3)	0
Hypoproteinemia	2(14.3)	0
Nausea	2(14.3)	0
Vomiting	2(14.3)	0

Abbreviations: TRAE = treatment-related adverse event.

Note: Data cut-off: June 29, 2023; AEs graded according to NCI CTCAEv.5.0.

Source: Company data

Efficacy Profile. The efficacy analysis presented below encompasses data from the dose escalation phase of IAE0972, involving a total of 14 enrolled subjects, of which nine were evaluable until the data cut-off date. An evaluable subject was defined as a subject who had undergone at least one tumor assessment after baseline. Among the nine evaluable subjects, four heavily pretreated patients who failed and became resistant to all previous chemotherapies/immunotherapies (two patients with rectal cancer, one with GC, and one with glioblastoma) exhibited SD, with the tumor volume of a GC patient in Cohort 4 reduced by 20%. The DCR was calculated to be 44.4%.

Group	Patient	Previous Treatment	Efficacy
0.01mg/kg	Rectal cancer combined with lung metastasis	Resistant to standard mFOLFOX6 regimen and CapeOX regimen, followed by irinotecan + raltitrexed + bevacizumab; furoquinitinib, regorafenib-targeted drugs	Achieved SD at first efficacy evaluation after 2 cycles of IAE0972
0.1mg/kg	Glioblastoma combined with metastasis to pleura, bone and pleural effusion	Resistant to radiation therapy with temozolomide, followed by bevacizumab + temozolomide	Achieved SD at first efficacy evaluation after 2 cycles of IAE0972
0.3mg/kg	Gastric cancer combined with liver metastasis	Resistant to Nivolumab in combination with tegeo + oxaliplatin, later changed to selective tumor arterial continuous perfusion with paclitaxel in combination with raltitrexed (later changed to oxaliplatin) combined with Nivolumab immunotherapy; oral apatinib when discharged, during which systemic chemotherapy with cisplatin was administered, but disease progressed; given docetaxel in combination with nedaplatin chemotherapy	Achieved SD at first efficacy evaluation after 2 cycles of IAE0972 with tumor shrank by 20%
1.0mg/kg	Rectal cancer combined with lung metastasis and lymph node metastasis	Recurrence after first time resection; disease progressed with lung, lymph node metastasis after second time resection	Achieved SD at first efficacy evaluation after 2 cycles of IAE0972

Abbreviations: SCLC = small cell lung cancer; PR = partial response; SD = stable disease; PD = progressive disease; NA = not available.

Note:

Data cut off on June 29, 2023.

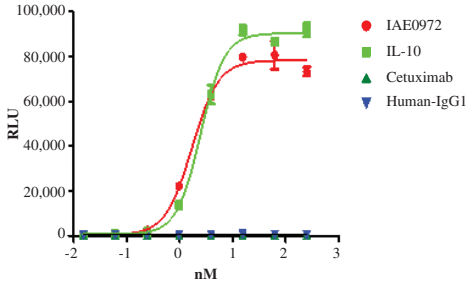
Source: Company data

Conclusion. The preliminary efficacy results showed encouraging antitumor activities when IAE0972 was administered as a monotherapy, even in heavily pretreated tumor types. Furthermore, our safety data indicated that IAE0972 can be safely administered to subjects at doses up to 2.5 mg/kg on a weekly basis.

Summary of Preclinical Data

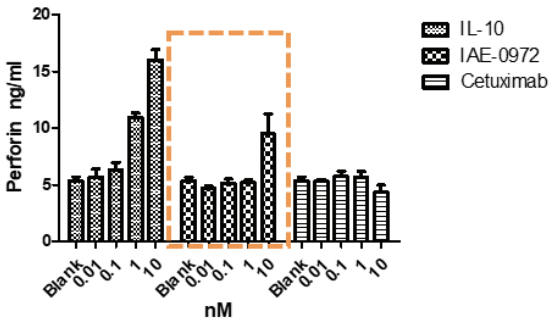
The preclinical study results demonstrate that IAE0972 exhibits equimolar binding capacity to the IL-10R, similar to IL-10, and can selectively activate IL-10/IL-10R signaling. *In vitro* studies using peripheral blood mononuclear cells demonstrated that IL-10 significantly stimulated the secretion of perforin by CD8+ T cells in a concentration-dependent manner. Perforin is a pore forming cytolytic protein found in the granules of cytotoxic T lymphocytes and NK cells, which plays a key role in granzyme-mediated programmed cell death, and in defense against tumor cells. At high concentrations, the IAE0972 antibody also significantly stimulated perforin secretion by CD8+ T cells, while cetuximab failed to induce such secretion.

IAE0972 activates IL-10 Reporter HEK-293 cell luciferase expression



	IAE0972	IL-10
EC_{50}	1.719	2.502

perforin cytokine secretion of CD8+T Cell

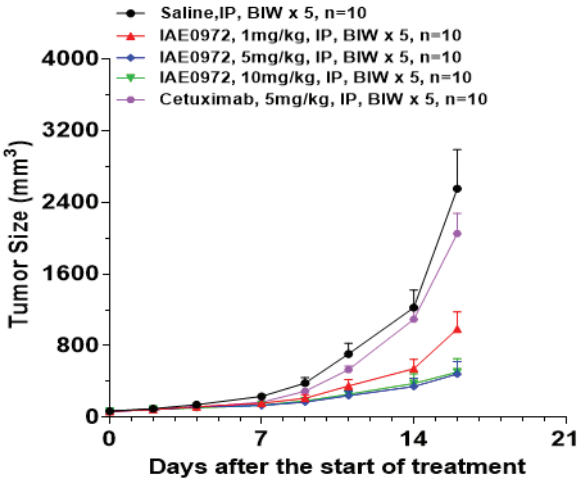


Source: Company data

In vivo data of the preclinical study showed that IAE0972 was well tolerated up to 6 mg/kg in cynomolgus monkeys, which is 300 times the safe dosage of IL-10 cytokine therapy. Also, no obvious EGFR-related skin toxicity, no significant organ changes for spleen, thymus, adrenal gland, axillary lymph nodes, and thyroid gland, as well as no significant changes for levels of IL-2, tumor necrosis factor-alpha ("**TNFα**") and Interferon-gamma ("**IFNγ**") were observed in the cynomolgus monkey repeated-dose toxicity studies.

IAE0972 also showed an excellent tumor inhibition effect in the C57BL/6 mouse allograft tumor model. Specifically, it showed a TGI rate of 83%, which is significantly higher than cetuximab. The *in vivo* data obtained from the study revealed significant tumor inhibition by IAE0972 at doses of 1mg/kg, 5mg/kg and 10mg/kg, resulting in TGI rates of 63.05%, 83.26% and 82.46%, respectively. The TGI effect of the 5mg/kg dose of IAE0972 was comparable to

that of the 10mg/kg dose. In comparison to the control group, the cetuximab 5mg/kg group did not exhibit a significant TGI effect, whereas the IAE0972 1mg/kg group demonstrated a significantly superior TGI effect when compared to cetuximab, despite using a much lower dose.



Source: Company data

Clinical Development Plan

We are currently implementing a comprehensive clinical trial development plan in China and the U.S. targeting a wide range of cancer indications for our product candidate IAE0972.

Fast-to-Market Strategy

We have strategically chosen to conduct Phase II clinical trials of IAE0972 in the treatment of two cancer indications, namely HNSCC and CRC, which have few or no effective treatment options for heavily pretreated patients. We believe that these strategic choices will accelerate the regulatory approval process and facilitate the commercial launch of IAE0972.

- 2L HNSCC

According to Frost & Sullivan, there were approximately 292.2 thousand new cases of 2L advanced HNSCC globally in 2022, and the number is projected to reach 358.6 thousand in 2030. In 2022, there were approximately 44.7 thousand new cases of 2L advanced HNSCC in China, and the number is projected to reach 53.0 thousand in 2030. The five-year survival rate of advanced HNSCC is approximately 40%. EGFR overexpression has been consistently observed in the majority of HNSCC cases, contributing to resistance against cytotoxic agents and radiotherapy, which ultimately leads to a poor prognosis. As a result, EGFR targeted therapy holds considerable promise as a second-line treatment option.

While immune checkpoint inhibitors have taken the forefront as first-line treatment options in major jurisdictions such as the U.S., EGFR inhibitor, particularly cetuximab, continue to hold significance as a viable second-line option for patients who have experienced progression on immune checkpoint inhibitors. Nonetheless, since chemotherapy continues to be an important first-line treatment option, most patients receive a combination of immune checkpoint inhibitors and chemotherapy. This highlights the existing medical needs for the development of treatments for patients who have either failed to respond or cannot tolerate immune checkpoint inhibitors in combination with chemotherapy. As of the Latest Practicable Date, despite the positive efficacy demonstrated by anti-EGFR antibodies, none of them have received regulatory approval from authorities such as the NMPA or the FDA for second-line treatment after the failure of immune checkpoint inhibitors in combination with chemotherapy.

Given the outlook for EGFR inhibitors, we plan to initiate a Phase II trial aimed at assessing the efficacy of IAE0972 as a monotherapy for patients diagnosed with advanced HNSCC who have undergone frontline treatment includes immunotherapy. We have initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first HNSCC patient in July 2023.

- 3L CRC

CRC ranks as the third most frequently diagnosed cancer worldwide and the second leading cause of cancer-related mortality, as reported by the World Health Organization GLOBOCAN database. According to Frost & Sullivan, there were approximately 353.3 thousand new cases of 3L advanced CRC globally in 2022, and the number is projected to reach 452.2 thousand in 2030. In 2022, there were approximately 86.0 thousand new cases of 3L advanced CRC in China, and the number is projected to reach 111.8 thousand in 2030. The five-year survival rate of advanced CRC can be as low as 16%. The gravity of this disease and the limited therapeutic options available highlight the urgent need for new treatments to address the significant unmet medical needs of CRC patients, particularly those with metastatic CRC who have experienced disease progression after three or more prior lines of therapy, including EGFR antibody-based treatments.

Anti-EGFR monoclonal antibodies, such as cetuximab or panitumumab, are increasingly utilized in the first- or second-line treatment of RAS wild-type metastatic CRC patients. However, as patients progress beyond the second-line therapies, some individuals may no longer be suitable for additional chemotherapy due to poor performance status or personal preferences. Nevertheless, a considerable portion of patients still qualify for further anti-EGFR therapy despite the limited availability of standard treatment options. The potential role of rechallenge with anti-EGFR therapy, especially for patients who have previously shown a positive response, is often considered. Rechallenging with anti-EGFR therapy in former responders exhibiting wild-type RAS in circulating tumor DNA assay after an interval of more than eight months represents a promising treatment approach.

While EGFR antibodies have demonstrated encouraging efficacy signals in general, no EGFR antibody has yet obtained marketing approval from regulatory authorities such as the NMPA or the FDA specifically for CRC rechallenge. IAE0972, an EGFR/IL10 immunocytokine, is expected to exhibit improved response rates in patients with RAS wild-type CRC beyond the second line treatment. To assess its efficacy as a monotherapy in patients with advanced CRC as third-line or later treatment, we have initiated a Phase II clinical trial of IAE0972 as monotherapy in China, and enrolled the first CRC patient in December 2023.

Major Indications

We are currently exploring the possibility of broadening the indications of IAE0972 to encompass a wider range of patient populations, such as those diagnosed with 2L squamous NSCLC and 1L HCC.

- 2L squamous NSCLC

Lung cancer ranks highest in terms of incidence among all cancer types in China, with NSCLC comprising approximately 85% of the lung cancer cases, according to Frost & Sullivan. There were approximately 328.5 thousand new cases of 2L advanced squamous NSCLC globally in 2022, and the number is projected to reach 422.3 thousand in 2030. In China, there were approximately 138.8 thousand new cases of 2L advanced squamous NSCLC in 2022, and the number is projected to reach 181.2 thousand in 2030. The five-year survival rate of advanced NSCLC is extremely low, at approximately 9%.

Clinical data has indicated that the combination chemotherapy involving necitumumab, an anti-EGFR antibody, exhibits antitumor effects for lung cancer patients. As such, the FDA approved necitumumab under the brand name Portrazza for use with gemcitabine and cisplatin in previously untreated metastatic squamous NSCLC. Our IAE0972, which is an immunocytokine that targets EGFR carrying IL-10 payloads, holds potential for even greater efficacy compared to necitumumab, while maintaining a manageable safety profile.

The first-line treatment for NSCLC involves a combination of chemotherapy and PD-1 immunotherapy. Unfortunately, primary and acquired drug resistance to PD-1 treatment can eventually lead to disease progression, leaving NSCLC patients with limited options. Currently, as of the Latest Practicable Date, no targeted therapy or immunotherapy has obtained regulatory approval from authorities for second-line treatment after immune checkpoint inhibitors in combination with chemotherapy have failed to treat NSCLC. Due to its potential of simultaneously simulating both innate and adaptive immunity in patients who suffer from primary or acquired drug resistance to immunotherapies, especially acquired drug resistance to immune checkpoint inhibitors caused by T cell exhaustion, our IAE0972 can potentially address these medical needs.

In China, our upcoming plans involve initiating a Phase II clinical trial for IAE0972 in combination with docetaxel in squamous NSCLC patients as second-line treatment. We plan to submit an IND application and after receiving the approval, enroll the first patient in the trial in the third quarter of 2024. Subsequently, in the second half of 2026, we intend to commence a Phase III trial for IAE0972. These initiatives signify our commitment to advancing the development and assessment of IAE0972 as a treatment option for lung cancer patients in China.

- 1L HCC

HCC ranks the second deadliest cancer and the fourth most prevalent malignant tumor in China, according to Frost & Sullivan. Overexpression of EGFR has been observed in around 40%-70% of conventional HCCs in most scientific research studies. According to Frost & Sullivan, there were approximately 716.1 thousand new cases of 1L advanced HCC globally in 2022, and the number is projected to reach 897.2 thousand in 2030. In 2022, there were approximately 331.9 thousand new cases of 1L advanced HCC in China, and the number is projected to reach 409.5 thousand in 2030. For late stage HCC, the five-year survival rate can be extremely low, at approximately 4%.

For late-stage HCC, systemic therapies are primarily recommended for first-line treatments, two major classes of which are small molecule targeted drugs, such as NEXAVAR® (sorafenib), LENVIMA® (lenvatinib), and immune checkpoint inhibitors, such as PD-1/PD-L1 inhibitors. Sorafenib has become the standard of care for patients with advanced HCC and also for those progressing after loco-regional therapies. It is an inhibitor with reported activity against Raf-1, B-Raf, VEGFR2, PDGFR, c-Kit receptors, targeting the EGFR-Ras-MAPKK pathway.

By targeting EGFR while carrying IL-10 payloads, IAE0972 may offer higher efficacy and a better safety profile compared to the current first-line treatments. Our plans entail conducting Phase II and Phase III clinical trials to evaluate the efficacy of IAE0972 in combination with chemotherapy, in comparison to lenvatinib, as first-line treatment for advanced HCC in China. In November 2023, we received the IND approval from the NMPA for conducting Phase II and Phase III clinical trials of IAE0972 in combination with lenvatinib in patients with locally advanced or metastatic HCC as first-line treatment. The enrollment of the first patient in a Phase II trial is scheduled in the second quarter of 2024. Following that, we anticipate conducting a Phase III trial to delve further into the potential of IAE0972 in HCC.

Global Strategy

We are carrying out a global strategy in the clinical development of IAE0972. In the U.S., we have obtained an IND approval for investigating IAE0972 as a monotherapy in Phase I and Phase II clinical trials in advanced malignant tumors in December 2021. Because the Phase I and Phase II clinical trial designs approved by the NMPA and the FDA are the same including the site (located in China) and PI of the clinical trials, we plan to leverage clinical data

collected in the Phase I trial in China, carefully decide our clinical development plan in the U.S., communicate with the FDA regarding the Phase II clinical trial design, and upon reaching an agreement with the FDA regarding the trial design, initiate Phase II clinical trials in the U.S. according to the FDA approved clinical trial design either by ourselves or through international collaboration. We may conduct clinical trials by ourselves, or through third party CROs or international collaborators. Alternatively, depending on the specific clinical stage and therapeutic regimen we carefully decide upon in the future, we will submit a new IND application to the FDA when new IND approval is required. Considering the costs, we decided to proceed with clinical trials in China first. As of the Latest Practicable Date, we had not commenced the clinical trials in the U.S. and had not planed to commence the trials in the U.S. within the coming six months.

Although the FDA has issued the IND approval and accepted that Phase I and Phase II clinical trials of IAE0972 can be conducted in China, we cannot guarantee that the FDA will accept our clinical results generated in China to support future clinical trials in the U.S., and we may face difficulties and incur additional costs thereof. For details, see "Risk Factors — Risks Relating to Government Regulations — We Primarily Conduct Clinical Trials for Our Drug Candidates in China, While FDA or Comparable Foreign Regulatory Authorities May Not Accept Data From Such Trials" in this document.

Licenses, Rights and Obligations

IAE0972 was developed by us, and we maintain the global rights to develop and commercialize this drug candidate.

Material Communications with Competent Authorities

The material communications with the relevant competent authorities on all ongoing and completed clinical trials in respect of the Core Product IAE0972 are as follows:

- In December 2021, we received the IND approval for conducting Phase I and Phase II clinical trials of IAE0972 for advanced solid tumors from the FDA.

- In January 2022, we received the IND approval for conducting Phase I and Phase II clinical trials of IAE0972 for advanced solid tumors from the NMPA.

- In September 2023, we conducted an interview with a senior examiner of the NMPA with the attendance of professional parties, which reconfirmed, amongst others, that the Phase I clinical trial of IAE0972 has been completed, and based on the safety and efficacy data from the Phase I clinical trial, that the NMPA had no objection for us to commence the planned Phase II clinical trials of IAE0972 as a monotherapy for 2L HNSCC and 3L CRC.

- In November 2023, we received the IND approval for conducting Phase II and Phase III clinical trials of IAE0972 in combination with lenvatinib for locally advanced or metastatic HCC from the NMPA.

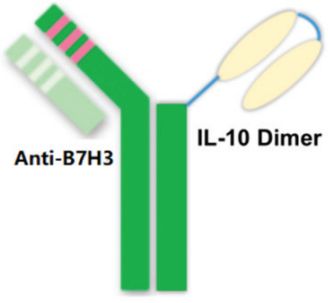
- In December 2023, we conducted a phone interview with the Director of Nanjing Inspection Branch, Jiangsu Provincial Medical Products Administration, which is a provincial branch regulated by the NMPA, with the participation of professional parties (the "**Regulatory Phone Interview**"). During the Regulatory Phone Interview, the Director confirmed that approval of drugs is managed by the approval number, which corresponds to the registration certificate of a drug, and the approval will encompass any different indications or combination therapy approved for marketing. In addition, if there are new indications or combination therapy for a marketed drug, the company can also make a supplemental application, but the company will not receive a new approval number for the same drug. Therefore, the monotherapy and combination therapy of the same drug for different indications, once approved by the NMPA, will be regulated under the same drug certificate in China.

We have not received any concerns or objections from the NMPA or the FDA related to receiving IND approvals, conducting Phase II clinical trials, or executing any other clinical development plans as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IAE0972 SUCCESSFULLY

Clinical-Stage Product IBB0979 (B7H3/IL-10 antibody-cytokine fusion protein)

IBB0979 is a clinical stage, dual-moiety, anti- B7 homolog 3 protein ("**B7H3**") antibody-IL-10 homodimer bifunctional fusion protein for immune cell activation. It is designed to bind to B7H3 and trigger blockage of downstream signaling pathways that participate in TME shaping and development, and deliver IL-10 to activate CD8+ T cells in the TME. The diagram below illustrates the structure of IBB0979:



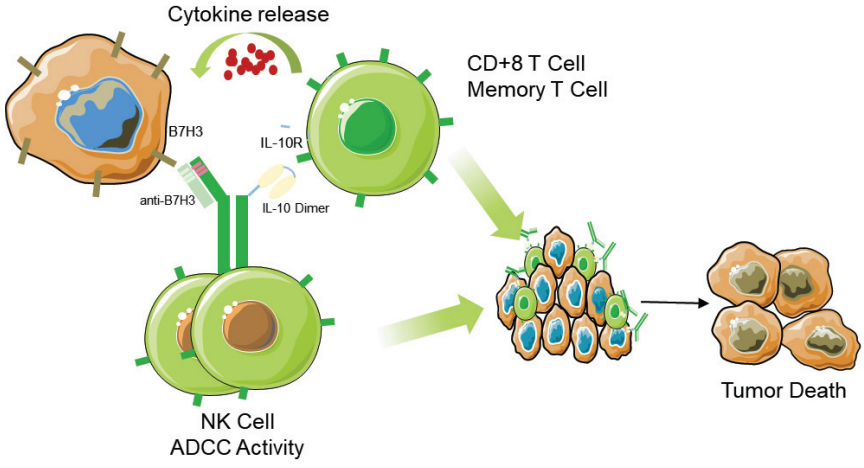
Source: Company data

We have obtained IND approvals from the NMPA and FDA for conducting Phase I and Phase II clinical trials of IBB0979 in locally advanced or metastatic solid tumors on November 2, 2022 and October 27, 2022, respectively. As of the Latest Practicable Date, we were investigating IBB0979 in a Phase I clinical trial to evaluate the safety, tolerability and preliminary efficacy of IBB0979 in patients with locally advanced or metastatic solid tumors in China. We expect to complete the Phase I clinical study in the fourth quarter of 2024 and enter the Phase II stage in the first quarter of 2025.

Mechanism of Action

B7H3, also known as CD276, a newly identified immune checkpoint protein member of the B7 family, is a popular target for cancer immunotherapy because it is overexpressed in tumor tissues and participating in TME shaping and development while showing limited expression in normal tissues due to its post-transcriptional regulation by microRNAs. It is overexpressed in many cancer types and is often associated with both negative prognosis and poor clinical outcome in patients. Researches revealed that in malignant tissues, B7H3 plays an important role in inhibiting tumor antigen-specific immune responses.

IBB0979 consists of an anti-B7H3 antibody fragment and a IL-10 homodimer. By targeting B7H3, the anti-B7H3 antibody fragment blocks the immunosuppressive signaling pathways in TME and enrich the IL-10 at the targeted tumor lesion. IL-10 will activate B7H3 specific CD8+ T cells to fight against the tumor.



Source: Frost & Sullivan Report

Market Opportunities and Competition

We believe IBB0979 has potential for the treatment of SCLC and mCRPC and plan to proceed the product into Phase II clinical trials.

SCLC

Lung cancer can be broadly categorized into two types: small cell lung cancer ("**SCLC**") and NSCLC. SCLC is a malignant tumor with high heterogeneity and invasiveness, accounting for 15% of lung cancer. In China, the number of SCLC cases is projected to increase to 166.5 thousand in 2026 with a CAGR of 3.2% from 2022 to 2026, and 185.7 thousand by 2030, with a CAGR of 2.8% from 2026 to 2030. The number of new SCLC cases worldwide increased from 314.1 thousand to 349.6 thousand from 2018 to 2022, with a CAGR of 2.7%. It is anticipated that by 2026 and 2030, the number of worldwide SCLC cases will reach 389.9 thousand and 432.7 thousand, respectively. The current drug treatment paradigm for SCLC in China involves applying EP/EC for LS SCLC and EP/EC/IP/IC for ES SCLC as the first-line treatment, with tyrosine kinase inhibitors ("**TKIs**") drugs being recommended as the 3rd-line treatment only in China.

Due to the asymptomatic nature and rapid progression of the disease, most SCLC patients are diagnosed in the extensive-stage (ES, which refers to the late-stage of SCLC with distant metastases), resulting in poor prognosis. The specific medical treatments such as chemotherapy alone or in combination with PD-1/PD-L1 inhibitors (such as atezolizumab, durvalumab and serplulimab), are recommended in the ES-SCLC.

Although the combination of chemotherapy with PD-L1 inhibitors (atezolizumab, durvalumab) has been approved for treating ES-SCLC, its clinical benefit is limited, with only a median overall survival improvement of two months compared to chemotherapy alone (12.3-13.0 months vs 10.3 months). Furthermore, serplulimab (a PD-1 inhibitor) combined with chemotherapy is currently restricted to treating MSI-H SCLC, indicating few options for immunotherapy in ES-SCLC. Consequently, many patients are unable to benefit from current treatments, and with relapse and drug resistance being common, the treatment options for R/R SCLC are limited to chemotherapy, with a median OS of only 4 to 5 months. Therefore, there is an urgent need for more effective treatments to improve survival outcomes for both primary and subsequent lines of treatment in ES-SCLC.

mCRPC

Prostate cancer is an epithelial malignant tumor that typically appears in the prostate gland and is the most common form of malignant tumor in the male genitourinary system. It primarily affects individuals over 65 years of age, and its progression is slow, with the early stages being mostly asymptomatic. However, once it migrates or metastasizes, the condition can become more severe, debilitating, and bearing a heavy disease burden for the patient.

In China alone, new cases of prostate cancer numbered 127.9 thousand in 2022, and is expected to increase to 147.8 thousand in 2026 and further to 170.6 thousand by 2030, representing a CAGR of 3.7% between 2026 and 2030. Globally, prostate cancer is one of the most prevalent cancer types, with an estimated 1,497.2 thousand new cases in 2022, expected to increase to 1,688.6 thousand in 2026 and 1,892.3 thousand in 2030.

In the case of mCRPC, endocrine drug therapy (such as mocetinostat) and chemotherapy are mainly recommended for first-line treatment. Immunotherapy options like PD-1 inhibitors, such as pembrolizumab, are approved for mCRPC patients with MSI-H/dMMR tumors. However, there is a significant unmet clinical need for effective therapies with improved efficacy, capable of benefitting more patients, in the mCRPC segment. Urgent strategies are therefore required.

Competitive Landscape

According to Frost & Sullivan, there are currently no approved B7H3-targeted immunotherapies indicated for the treatment of cancer. Globally, there are 16 products in various stages of clinical development, with the most advanced candidates undergoing Phase III clinical trials. In China, ten products targeting B7H3 are currently under clinical development, with the most advanced product in Phase II. Globally, among all product candidates targeting B7H3, IBB0979 stands out as the only immunocytokine currently undergoing investigation in clinical trials.

Competitive Advantages

IBB0979 is a B7H3/IL-10 immunocytokine developed based on our AIC™ Platform. It shares the same synergistic mechanism and structural design as IAE0972. The dual targeting offered by IBB0979 holds tremendous potential for expanding our indication footprint in solid tumors.

Advantages in terms of molecular design

IBB0979 adopts a mechanism of combining tumor-associated antigens and immune checkpoints, which represents a new approach in cancer treatment.

- B7H3 is abnormally highly expressed in various cancers while being expressed at low levels in normal human tissues. Available data from immunohistochemistry assays demonstrate that B7H3 is highly expressed in tumor cells and blood vessels in breast, brain, rectal colon, kidney, lung and pancreatic cancers but expressed at lower levels in normal tissues and blood vessels, making it an ideal target for developing cancer treatment.

- As a member of the B7-CD28 family of immunomodulatory proteins, B7H3 plays a crucial role in tumor development and immune escape. Its high expression in tumor tissues is often associated with tumor growth, reduced infiltrating lymphocytes in the tumor area, and T cell and NK cell-mediated antitumor immunosuppression. B7H3 has been demonstrated to be associated with tumorigenesis and progression of various types of cancer, including melanoma, glioma, lung cancer, pancreatic cancer, ovarian cancer, breast cancer, gastric cancer, and colon cancer, and is linked with poor prognosis in these tumors.

- While several drugs are currently being developed to target B7H3, none have yet received marketing approval. The range of drug types under development includes mAbs, dual antibodies, antibody-drug conjugates ("**ADCs**") and chimeric antigen receptor T-cell ("**CAR-T**") therapies. Among them, DS-7300A, a B7H3 ADC, is the most extensively studied drug and has shown promising preliminary efficacy, with ten confirmed partial remissions and five pending confirmed partial remissions.

The asymmetric heterodimer structure design of IBB0979 effectively address heavy chain mismatch and druggability issues.

- IBB0979 features a monovalent design at the antibody end, whereas IL-10 exhibits a naturally occurring homodimeric structure, providing natural immune cell activating activity.

- Additionally, IBB0979 incorporates a knobs-into-holes configuration that effectively addresses the heavy chain mismatch, thereby enhancing its druggability in terms of CMC considerations.

- IBB0979, developed through our asymmetric immunocytokine cell line technology, achieves an expression amount of 4g/L. With one-step affinity chromatography, it reaches approximately 86% purity and offers a final yield of around 60%, highlighting its strong commercial scalability.

Advantages in terms of safety and efficacy based on preclinical studies

- IBB0979 demonstrated complete tumor remission across a range of tumor models, achieving doses of 0.3-1 mg/kg. In cynomolgus monkeys, it exhibited a tolerated dose of 6mg/kg, significantly widening the safety and efficacy window compared to other B7H3-targeting drugs.

- IBB0979 exhibits structural stability, superior targeting capabilities, and a longer half-life when compared to an IL-10 cytokine product. Cynomolgus monkeys tolerated IBB0979 at a dose of 6 mg/kg, which is significantly higher than the 10-20 μg/kg tolerated by IL-10 cytokines alone. This represents at least a remarkable 300-fold increase in the therapeutic window.

Summary of Clinical Trial Results

Phase I clinical trial in patients with advanced solid tumors

Trial Design. This is a Phase I clinical trial designed to characterize the safety, tolerability, and preliminary effectiveness of IBB0979 in patients with locally advanced or metastatic solid malignant tumors. This trial is conducted with IND approvals from both the NMPA and FDA. The trial is currently being conducted in China. The study consists of a Dose Escalation Phase (Phase Ia) to determine the MTD of escalating doses of IBB0979, and a Dose

Expansion Phase (Phase Ib) to further define safety and initial effectiveness of IBB0979 at the dose established in Phase Ia. Each phase of the study includes: the screening period (28 days after the subject signs the informed consent form and before the first administration of the study drug), the treatment period (the first administration of the study drug until any endpoint event occurs), and the follow-up period. For the dose escalation phase, there are eight dosing cohorts, with dose levels ranging from 0.01 mg/kg QW to 10.0 mg/kg QW by intravenous injection.

Trial Status. We have initiated patient enrollment in July 2023 in China, and plan to complete the Phase I study in the fourth quarter of 2024.

Clinical Development Plan

We are executing a comprehensive clinical trial development plan in China and the U.S. targeting an array of cancer indications for our IBB0979.

Fast-to-Market Strategy

- 2L ES SCLC

ES-SCLC is an extremely aggressive form of cancer, and despite initially high response rates to first-line therapy, disease progression often occurs within a mere six months. Furthermore, there are very limited treatment options available for relapsed SCLC, highlighting a critical and urgent medical need for more effective therapies that can provide lasting benefits beyond the second line of treatment.

One promising avenue of research involves B7H3, a protein that is overexpressed in various cancers, including SCLC, and has been associated with a poor prognosis. DS-7300, an ADC consisting of a humanized anti-B7H3 antibody and deruxtecan, has shown great potential in an ongoing Phase I/II study involving 19 SCLC patients. Preliminary results showed encouraging ORR and DoR. These findings provide promising evidence of DS-7300's clinical activity.

Building upon this success, IBB0979, an immunocytokine targeting B7H3 and IL-10, is expected to further enhance the ORR while potentially offering improved safety. To evaluate the effectiveness of IBB0979 as a standalone treatment for patients with advanced-stage (≥2L) ES-SCLC, we plan to initiate a Phase II trial in China. The enrollment of the first patient is anticipated in the first quarter of 2025.

Major Indication

We are evaluating IBB0979 for the treatment of some of the most prevalent cancer types, such as mCRPC, considering that the combination therapy of B7H3 monoclonal antibody such as enoblituzumab (MGA271), and ADCs targeting B7H3 such as MGC018 and DS-7300, have demonstrated promising preliminary efficacy.

- 1L mCRPC

Prostate cancer ranks as the second most frequently diagnosed cancer and the sixth leading cause of cancer-related deaths among men worldwide. Despite the initial efficacy of androgen deprivation therapy in advanced prostate cancer, almost all patients eventually develop resistance, leading to biochemical and clinical evidence of treatment failure. This state is referred to as castration-resistant prostate cancer ("**CRPC**"). Over the past decade, researchers have identified various categories of treatments for CRPC, including chemotherapy, novel hormonal agents, and immune- and targeted therapies.

B7H3, a protein highly expressed in many prostate cancers, plays a role in modulating antitumor immune responses and is associated with a poor prognosis. MGC018 from, MacroGenics is a mAb targeting B7H3, currently undergoing Phase II investigation for mCRPC and ES-SCLC. Furthermore, DS7300a and MGC018, anti-B7H3 ADCs, have demonstrated promising outcomes in Phase I trials involving mCRPC subjects. Targeting B7H3 has emerged as an innovative therapeutic approach in the management of mCRPC.

IBB0979, an immunocytokine combining B7H3 and IL-10, holds potential as a treatment option to further enhance outcomes in mCRPC. We plan to enroll the first patient in the Phase II study of IBB0979 in combination with enzalutamide in China in the first quarter of 2025.

Global Strategy

We are carrying out a global strategy in the clinical development of IBB0979. In the U.S., we have obtained an IND approval for IBB0979 for conducting Phase I and Phase II clinical trials in solid tumors in October 2022. Because the clinical trial designs approved by the NMPA and the FDA are the same, we expect to leverage the Phase I clinical data collected in China to proceed with clinical development in the U.S. We will proceed clinical development in the U.S. either by ourselves or through collaboration with third parties. As of the Latest Practicable Date, we had not commenced the clinical trials in the U.S. and had not planned to commence the trials in the U.S. within the coming six months.

Licenses, Rights and Obligations

IBB0979 was developed by us, and we maintain the global rights to develop and commercialize this drug candidate.

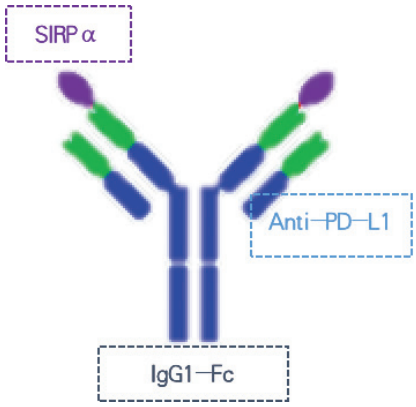
Material Communications With Competent Authorities

We have not received any concerns or objections from the NMPA and FDA related to our clinical development plans as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBB0979 SUCCESSFULLY

Clinical-Stage Product IBC0966 (PD-L1/SIRPα antibody fusion protein)

IBC0966 is a clinical stage, anti- PD-L1 antibody-SIRPα bifunctional fusion protein that simultaneously stimulates both innate and adaptive immunity to achieve strong synergistic effects and induce long-lasting tumor-specific immune responses. It is designed to bind to PD-L1 and trigger blockage of the PD-1/PD-L1 signaling pathway to enable T cells to recognize and kill targeted cancer cells, and in the meantime deliver SIRPα to the targeted TME to interact with CD47 to block the "don't eat me" signal of macrophages for tumor cell killing. The diagram below illustrates the structure of IBC0966:



Source: Company data

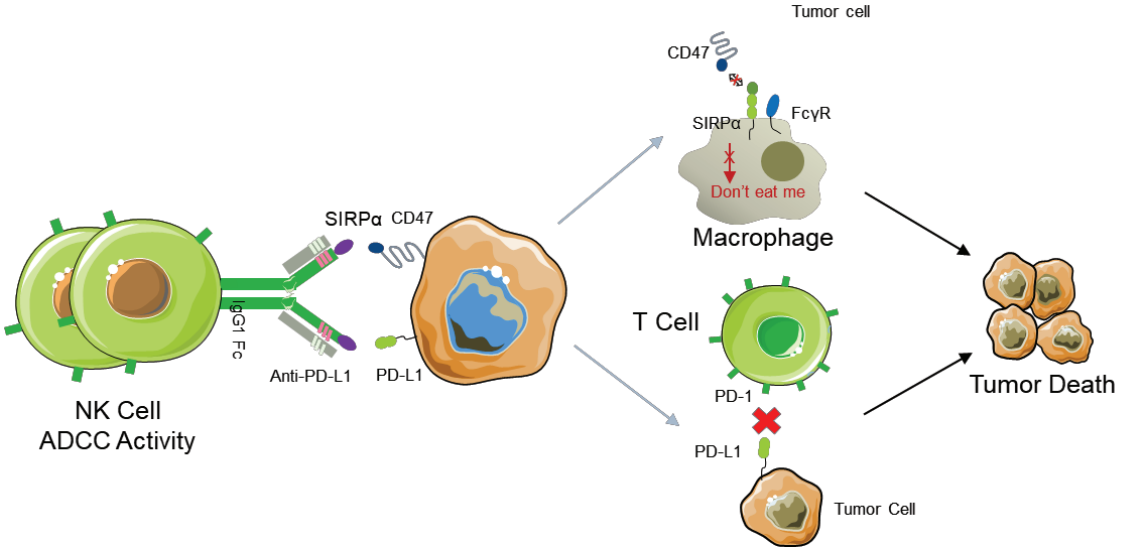
On March 17, 2021, we obtained the IND approval from the NMPA for conducting Phase I and Phase II clinical trials of IBC0966. We completed the Phase I study of IBC0966 as a monotherapy for advanced malignant tumors in December 2023, and expect to enter the Phase II clinical stage in the second quarter of 2024.

Mechanism of Action

SIRPα is a regulatory membrane protein that belongs to SIRP family. It interacts with CD47, which is usually over-expressed on tumor cells and trigger a signaling pathway called "don't eat me". This interaction negatively regulates the function of innate immune cells. Specifically, SIRPα diffuses laterally on the macrophage membrane and accumulates a phagocytic synapse to bind CD47 and signal "self", which inhibits the cytoskeleton-intensive process of phagocytosis by the macrophage. Therefore, blockade SIRPα from binding to CD47 will activate macrophage-mediated destruction against tumor cells that highly express CD47, and also present tumor antigens to activate the adaptive immune system.

The PD-1/PD-L1 pathway represents an adaptive immune resistance mechanism exerted by tumor cells in response to endogenous immune antitumor activity. PD-1 is expressed by all T cells during activation, which often shows high and sustained expression levels during persistent antigen encounter. Its ligand PD-L1 shows broad expression on tumor cells. Their engagement signals to prevent the immune system from attacking the tumor cells. Inhibitor that blocks the PD-1/PD-L1 pathway can prevent the cancer from evading the immune system attacks.

IBC0966 is a bifunctional antibody that targets both PD-L1 and CD47. It adopts a symmetrical mAb-Trap 2+2 molecular structure, and thus can avoid the potential mismatches between the light and heavy chains, which can improve the expression and purification yields and thus is suitable for industrial mass production. The SIRPα moiety of IBC0966 does not bind to human erythrocytes at all, which allows us to adopt an IgG1 structure that has enhanced antitumor activities through ADCC and ADCP activities. IBC0966's low systemic haematotoxicity also contributes to the anti-PD-L1 moiety, which binds to PD-1 with 45 times affinity of SIRPα to its target CD47. Through this design, IBC0966 is able to block "don't eat me" signal and PD-1/PD-L1 pathway, and thus simultaneously stimulates innate and adaptive immunity and exerts enhanced antitumor activities against tumor cells.



Source: Frost & Sullivan analysis

Market Opportunities

We plan to conduct a Phase II clinical trial of IBC0966 for NHL.

NHL

Lymphomas are a type of hematologic cancer that affects the lymphocytes, the cells of the immune system. There are two primary categories of lymphomas: Hodgkin's lymphomas and NHL. Non-Hodgkin lymphomas account for approximately 90% of all lymphoma cases and encompass various subtypes.

According to Frost & Sullivan, the global new cases of NHL reached approximately 569.4 thousand in 2022. It is estimated to rise to approximately 624.2 thousand in 2026 and 682.0 thousand in 2030. Incidence of NHL in China reached approximately 97.6 thousand in 2022. It is estimated to rise to approximately 107.3 thousand in 2026 and 117.0 thousand in 2030.

NHL treatment options, such as radiation therapy, chemotherapy, stem cell transplantation, and biologics, can lose their effectiveness due to drug resistance, resulting in R/R NHL that poses significant challenges with limited treatment options. In the case of R/R B-cell NHL, CD20-targeted therapy is typically recommended, but this option has limited efficacy and is susceptible to drug resistance and infusion-related reactions. While novel immunotherapies, such as PD-1/PD-L1 inhibitors, and targeted therapies, such as brentuximab, have been developed for R/R T-cell NHL, chemotherapy remains the primary treatment option, and there is a high demand for more specific treatment options. Similarly, the PD-1 inhibitor (sintilimab) has been tested for R/R NKTCL, but its complete response rate of 7.1% indicates limited efficacy. Therefore, there is an urgent need to introduce novel treatment options to address the medical needs of R/R NHL. For example, targeting SIRPα with novel options could potentially serve as a solution for T-cell NHL, addressing the unsatisfactory current treatment outcomes by enhancing innate immunity and promoting T cell response through activated macrophages.

Competitive Advantages

IBC0966 is the world's first PD-L1/SIRPα dual-target mAb-Trap molecule approved to enter clinical stage. It can achieve a differential binding of two targets and avoid binding to red blood cells and thus has an improved safety profile comparing to other CD47-targeting therapies. It targets two signaling pathways with synergistic mechanisms of action to activate both innate and adaptive immunity. Based on the excellent safety, efficacy and quality controllability, IBC0966 is currently in the Phase I clinical trial and has already demonstrated its initial safety and efficacy. IBC0966 has the potential to become a safer and more effective molecule in clinical practice, solving the current problem of drug resistance and ineffectiveness in solid tumors and hematological tumors.

In terms of molecular design, IBC0966 adopts a symmetrical mAb-Trap dual-target molecular structure, avoiding mismatches between light and heavy chains, with high expression and purification yields, and suitable for industrial mass production. In addition, the structure of SIRPα has undergone biological engineering to mutate certain amino acids to further optimize the quality of the product and the molecular stability.

IBC0966 showed high binding affinity for PD-L1 and thus improved the safety profile. IBC0966 does not bind to human red blood cells and thus does not cause erythrocyte agglutination or T cell apoptosis. Studies showed that there is a 45-fold difference in affinity between the PD-L1-binding end and the CD47-binding end, enabling the anti-PDL1 antibody moiety to further target the IBC0966 molecule to the TME and reducing the hematotoxicity of systemic cytotoxicity and providing a good safety profile. Preclinical data showed that cynomolgus monkeys tolerated IBC0966 well with a maximum tolerated dose of 50 mg/kg for a single dose and 5 mg/kg for repeated doses.

Furthermore, IBC0966 blocks CD47 and PD-L1-PD-1 signaling, which activates macrophages and CD8+ T cells, leading to the activation of tumor-specific T cells. It employs a more potent IgG1 isotype that acts as an ADCC and ADCP to mediate the killing of CD47/PD-L1-positive tumor cells and prevent tumor escape due to single target shedding. The death of tumor cells releases a large amount of tumor-associated antigens, which are presented to the adaptive immune system by antigen-presenting cells, changing the tumor microenvironment from "cold" tumors to "hot" tumors and activating the immune system to kill tumor cells more effectively. IBC0966 has shown a 91% tumor growth inhibition rate *in vivo*, which is significantly better than anti-PD-L1 mAb and its combination therapy.

Summary of Clinical Trial Results

Phase I clinical trial in patients with advanced malignant tumors

Trial Design. This was a Phase I open label study designed to evaluate the safety, tolerability, PK, immunogenicity, and preliminary efficacy of IBC0966 in patients with advanced malignant tumors who have failed standard treatment. The study included two phases: dose-escalation phase (Ia) and dose-expansion phase (Ib). Each treatment cycle was defined as four weeks. The DLT evaluation period was defined as 28 days following intravenous administration of the first dose of IBC0966 (Cycle 1). During the DLT evaluation period, IBC0966 was administered intravenously once weekly ("**QW**") for 0.025 mg/kg, 0.05 mg/kg and 0.1 mg/kg, 0.2 mg/kg, 0.4 mg/kg and Q2W for 0.8 mg/kg, 1.6 mg/kg and 3.2 mg/kg. Tumor assessments were performed every eight weeks (i.e., prior to dosing for Cycles 3, 5, 7, etc.). Patients enrolled in this study who did not experience a DLT or other unacceptable toxicity that necessitates permanent discontinuation of investigational product, may continue treatment for up to disease progression, initiation of alternative anti-cancer therapy, lost to follow-up, withdrawal of informed consent, death, or end of study.

The primary objective of Ia/Ib study of this trial was safety and RP2D. The secondary objective included assessing PK portfolio, immunogenicity, and preliminary efficacy. The secondary objective included PFS, OS, DCR, safety and immunogenicity.

Trial Status. We completed the Phase I study in December 2023.

Safety Profile. Among the 21 subjects enrolled in the Phase I study, all subjects experienced AEs with most of them were in Grade 1-2. Out of the 21 subjects, only 12 subjects experienced Grade 3-4 AEs, which were primarily related to decreased platelet count (9/12). The others experienced fatigue (1/12), abdominal bloating (1/12), pneumonia (1/12), decreased lymphocyte count (1/12), and hypokalemia (1/12).

Efficacy Profile. As of the cut-off date (September 5, 2023), 15 subjects were evaluable for the efficacy analysis. Evaluable subject was defined as a subject with at least one post-baseline tumor assessment. Of 15 evaluable subjects, one subject with lung cancer achieved PR and six subjects (one with breast cancer, one with Hodgkin's lymphoma, one with melanoma, one with ovarian cancer, and two with lung cancer) achieved SD. The DCR was 46.7%.

The table below shows the detailed profile of previous treatment for the patients achieving best response of PR and SD.

Group	Patient	Previous Treatment	Efficacy
0.05 mg/kg	Non-Hodgkin's lymphoma	Resistant to Vindesine Sulfate combined with Epirubicin and Asparaginase and Prednisone + Methotrexate+Methotrexate and 6-thioguanine + Vincristine combined with Daunorubicin and Prednisone and L-asparaginase (VDPL)+ Cytoxan combined with cytosine arabinoside and 6-thioguanine (CTA)+ Methotrexate and 6-thioguanine+fufang banmao capsule	Achieved SD in the first evaluation after two cycles of IBC0966 administration
0.4 mg/kg	Hodgkin's lymphoma	Resistant to Epirubicin combined with Bleomycin and Dacarbazine (ABVD)+ Tislelizumab + Sintilimab	Achieved SD in the first evaluation after two cycles of IBC0966 administration
1.6 mg/kg	Melanoma	Resistant to Docetaxel and carboplatin+ Docetaxel and cis-platinum+ Docetaxel+ Docetaxel and cis-platinum+ Toripalimab	Achieved SD after two cycles of IBC0966 administration
1.6 mg/kg	Ovarian cancer	Resistant to Docetaxel and carboplatin+ Docetaxel and cis-platinum+ Docetaxel+ Etoposide and cyclophosphamide+ Gemcitabine and cisplatin +Olaparib+ Niraparib+ Bevacizumab and paclitaxel+ bevacizumab and doxorubicin+ Bevacizumab and nab-paclitaxel+ Bevacizumab+ Bevacizumab and Niraparib+ Niraparib	Achieved SD after two cycles of IBC0966 administration
1.6mg/kg	Lung cancer	Resistant to Nedaplatin and nab-paclitaxel and Camrelizumab+ BC3402	Achieved SD after one cycle of IBC0966 administration
3.2mg/kg	Lung cancer	Resistant to pemetrexed and carboplatin combination therapy, crizotinib, and products in clinical trials	Achieved PR after two cycles of IBC0966 administration

Group	Patient	Previous Treatment	Efficacy
3.2mg/kg	Ovarian cancer	Resistant to paclitaxel and carboplatin combination therapy, radiotherapy for secondary and metastatic tumors, olaparib, fluzoparib, and bevacizumab and tirilizumab combination therapy	Achieved SD after two cycles of IBC0966 administration

Conclusion. IBC0966 exhibited a favorable safety profile in subjects with advanced or metastatic tumors and the preliminary efficacy results demonstrated encouraging antitumor activities for IBC0966 monotherapy in heavily pretreated patients.

Clinical Development Plan

We will strategically conduct Phase II clinical trials for conditional approval of IBC0966 for the treatment of R/R non-Hodgkin lymphoma ("**NHL**"). We believe that these strategic choices will accelerate the regulatory approval process and commercial launch of IBC0966.

- R/R NHL

R/R NHL continues to pose a significant clinical challenge. While autologous stem cell transplantation may cure some patients, the ORR to subsequent lines of treatment are suboptimal, and patients often face limited options. Although CAR-T therapy may offer long-term benefits to some patients, its impact remains limited by factors such as toxicity, cost, access, and relapse. Although checkpoint inhibitor has shown impressive activity in R/R Hodgkin lymphoma, the outcomes have been disappointing in NHL. The median ORR is approximately 20%, and complete or durable responses are infrequent, except for primary mediastinal B cell lymphoma.

In a Phase II study of anti-CD47 Magrolimab, patients with R/R NHL, including diffuse large B-cell lymphoma ("**DLBCL**") or follicular lymphoma, were administered magrolimab (anti-CD47 antibody) in conjunction with rituximab (anti-CD20 antibody) to assess safety and efficacy. Of the total patients, encouraging objective response and complete response rates were observed among patients with DLBCL and among those with follicular lymphoma. Therefore, the combination of magrolimab with rituximab therapy appeared to be safe and induced durable complete responses in patients.

IBC0966, a bifunctional antibody fusion protein blocking both CD47/SIRPα and PD-1/PD-L1 signaling pathways, is expected to provide improved clinical benefits. Our plan is to launch a Phase II trial in the second quarter of 2024 and evaluate the efficacy and safety of IBC0966 combination therapy for R/R NHL.

Licenses, Rights and Obligations

We acquired exclusive rights from ImmuneOnco Biopharmaceuticals (Shanghai) Inc. to develop, manufacture and commercialize IBC0966 in Greater China including mainland China, Hong Kong, Macau and Taiwan, and as well as 7.5% of interests in the overseas rights of IBC0966. For detailed information, see "— Collaboration Arrangement — Collaboration Agreement With ImmuneOnco in Relation to the Development of IBC0966" in this section.

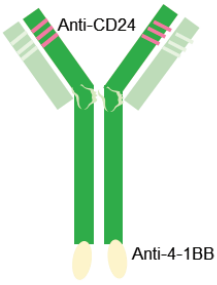
Material Communications with Competent Authorities

We have not received any concerns or objections from the NMPA related to our clinical development plans as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBC0966 SUCCESSFULLY

Clinical-Stage Product IBD0333 (4-1BB/CD24 BsAb)

IBD0333 is a clinical stage, 4-1BB and CD24 bsAb that simultaneously stimulates both innate and adaptive immunity to achieve strong synergistic effects with reduced hepatotoxicity. It is designed to bind to 4-1BB, a robust immune cell activator expressed by CD8+ T cells as well as DC cells, monocytes, B cells, mast cells, NK cells and neutrophils, and CD24, a target that plays a key role in tumor evasion in CD24-Siglec-10 axis and thus is highly expressed in many cancer types. The diagram below illustrates the structure of IBD0333:



Source: Frost & Sullivan analysis

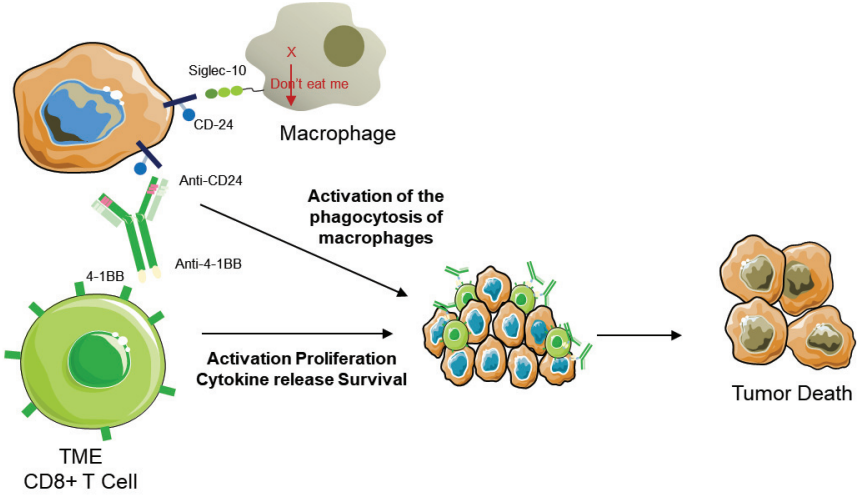
We have obtained IND approvals from the FDA on June 2, 2023 and from the NMPA on July 10, 2023. We initiated a Phase I clinical trial in March 2024 to evaluate its safety, tolerability, pharmacokinetic characteristics, and preliminary efficacy in patients with locally advanced/metastatic solid tumors in China. We expect to complete the Phase I study in the third quarter of 2025.

Mechanism of Action

4-1BB is a co-stimulatory molecule on immune cells. It is expressed on activated CD8+ T cells and forms a hexametric complex with the natural ligand 4-1BBL to stimulate T cell proliferation and activation. 4-1BB is also expressed on NK cells and enhances the ADCC effect of NK cells, promoting the proliferation of activated NK cells, eventually resulting in tumor cell apoptosis. In addition, 4-1BB is also highly expressed on DC cells, monocytes, B cells, mast cells, and neutrophils, which can trigger an activation signal in all these cell types. However, 4-1BB monoclonal antibody is hepatotoxic and requires TAA targeting to activate immune cells in the immune microenvironment more safely.

CD24 is a highly glycosylated protein with a small protein core that is linked to the plasma membrane via a glycosyl-phosphatidylinositol anchor. CD24 is primarily expressed by immune cells but is often overexpressed in human tumors. In cancer, CD24 is a regulator of cell migration, invasion and proliferation. Its expression is associated with poor prognosis and it is used as cancer stemness marker. CD24 can promote immune escape by interacting with the inhibitory receptor Siglec-10 on tumor-associated macrophages.

IBD0333 is a 4-1BB/CD24 bsAb. It adopts a symmetric structure of linking anti-CD24 moiety to the Fab region and anti-4-1BB moiety to the Fc region of both heavy chains of an IgG4 antibody backbone. The anti-CD24 moiety identifies CD24 expressed on the targeted tumor, and enrich anti-4-1BB terminus into the TME. As such, IBD0333 can specifically activate immune system in the tumor tissue and reduce systemic toxicity of 4-1BB.



Source: Frost & Sullivan Report

Competitive Advantages

Currently, there are no drugs targeting the 4-1BB pathway on the market, but there are multiple drugs under clinical development, including mAbs, bsAbs and CAR-T immunotherapy targeting 4-1BB. Among them, Urelumab (BMS-663513) and Utomilumab (PF-05082566) are two 4-1BB agonist mAbs that have made relatively fast progress. However, both drugs have certain limitations. Namely, Urelumab was observed to have dose-limiting hepatotoxicity and efficacy can be very limited at the safe dose. Utomilumab exhibited better safety and tolerability at higher doses than Urelumab, yet its efficacy was limited compared to Urelumab with only 3.8% overall ORR in solid tumor patients.

In addition to specifically enriching IBD0333 into the TME to reduce hepatoxicity, IBD0333 has additional unique structural designs that could potentially enable it to achieve superior safety and efficacy profile:

1. **Unique anti-4-1BB antibody design**. The 4-1BB signaling pathway is activated through binding to the 4-1BB and forming the 4-1BB trimer. The anti-4-1BB antibody in IBD0333 is an agonist antibody that targets a unique epitope so that when in absence of TAA, the anti-4-1BB antibody cannot stimulate the formation of the 4-1BB trimer. This design will reduce toxicity of 4-1BB in normal somatic cells, especially liver cells.

2. **Dual role of CD24**. When binding to CD24 overexpressed tumor cells, the anti-CD24 antibody of IBD0333 can specifically enrich anti-4-1BB antibody to the targeted site to induce a cross-linking effect between the anti-4-1BB antibodies. The cross-linking effect will enable anti-4-1BB antibodies to recognize 4-1BB and form the 4-1BB trimer to activate the T cells and other immune cells to kill tumor cells.

   CD24, expressed on the tumor cells, through its interaction with Siglec-10, expressed on macrophages, triggers a "don't eat me" signal that facilitate immune escape of tumor cells. By targeting CD24, the anti-CD24 antibody of IBD0333 blocks the signaling pathway of CD24/Siglec-10, and enable macrophage to recognize and kill tumor cells.

3. **The selection of IgG4 antibody backbone**. IBD0333 is a bsAb based on an IgG4. In general, IgG4 binds to its receptors with lower affinity (except for FcγRI), and is a poor inducer of Fc-mediated effector functions. Although existence of the anti-4-1BB antibody can block the Fc region's interaction with its receptors to some extent, Fc region of the antibody can still bind to its target to systemically activate immune cells that carries its receptors. By adopting IgG4 as its backbone antibody, IBD0333 further reduce the safety risk of 4-1BB.

Leveraging the synergistic effect between anti-CD24 moiety and anti-4-1BB moiety, IBD0333 is designed to specifically trigger the activation of immune cells, especially CD8+ T cells in the TME of the targeted tumor tissue, which can potentially lead to improved safety and efficacy portfolio.

Summary of Clinical Trial Results

Phase I clinical trial in patients with locally advanced/metastatic solid tumors or non-Hodgkin's lymphoma

Trial Design. This study is an open label, dose-escalation and extension Phase I clinical study to evaluate the safety, tolerability, PK profile, immunogenicity and preliminary efficacy of intravenous infusion of IBD0333 in subjects with locally advanced/metastatic solid tumors or non-Hodgkin's lymphoma, which is divided into two phases of dose-escalation and dose-expansion. Dose escalation is studied using an accelerated titration combined with a "3+3" design, starting with a starting dose of 0.05 mg/kg. The dose expansion is proposed to enroll six subjects with locally advanced/metastatic solid tumors or non-Hodgkin's lymphoma who have failed standard treatment or for whom no standard treatment is available or not applicable.

Primary endpoints of this study are DLT, MTD, RP2D and AEs. Secondary endpoints include PK profile, ADA assessment, ORR, DoR, PFS and OS.

Trial Status. We have obtained IND approvals from the FDA on June 2, 2023 and from the NMPA on July 10, 2023. We initiated the Phase I clinical trial in China in March 2024. As of the Latest Practicable Date, we had not commenced the clinical trials in the U.S. and had not planned to commence the trials in the U.S. within the coming six months.

Clinical Development Plan

We are executing a fast-to-market clinical development strategy in China and the U.S. targeting an array of cancer indications for our IBD0333. We plan to conduct Phase II clinical trials of IBD0333 for the treatment of cancer indications with few or no effective treatment options for heavily pretreated patients, including ovarian cancer ("**OC**"). We believe that this strategic choice will help accelerate IBD0333's regulatory approval process and commercial launch.

- *≥2L OC*

OC has a low cure rate and ranks fifth in terms of mortality rate among cancers affecting women. Approximately 75% of newly diagnosed patients are found to have advanced-stage disease, which partly explains the high mortality rate of this cancer. Even with aggressive treatment combining chemotherapy and debulking surgery, the five-year survival rate for advanced-stage disease is less than 30%.

Immunotherapy has emerged as a promising new option since immune checkpoint inhibitors (ICIs) have shown remarkable success in several cancers. However, unlike other immune-reactive cancers, OC has exhibited a response rate of only 10%-20% to immunotherapy in various clinical trials using anti-PD-1/PD-L1, and anti-CTLA-4 treatments. These poor results underscore the need for novel immunotherapeutic strategies.

Research on the 4-1BB+ T cell subset in ovarian cancer patients has revealed that this cell subset is distributed in three different locations: the TME, ascites, and peripheral blood. 4-1BB+ T cells are found to be in low level in peripheral blood, but they are predominantly found in ascites and even more so within the tumor. In addition, one patient with OC achieved a PR in a Phase I clinical trial of GEN1046 (PD-L1/4-1BB). Furthermore, a study showed a significant increase in the rate of apoptosis in the A2780 and HO-8910 PM OC cell lines after treatment with a monoclonal antibody targeting CD24.

We initiated the Phase I trial of IBD0333 for the treatment of advanced malignant solid tumor in China in March 2024, and expect to complete this trial in the third quarter of 2025. Based on the scientific finding and clinical data mentioned above, we intend to start a Phase II trial in the third quarter of 2025 to evaluate IBD0333 as a monotherapy in OC patients.

Licenses, Rights and Obligations

IBD0333 was developed by us, and we maintain the global rights to develop and commercialize this drug candidate.

Material Communications With Competent Authorities

We have not received any concerns or objections from the NMPA and FDA related to our clinical development plans as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBD0333 SUCCESSFULLY.

IND-Enabling Stage Pipeline Products

In addition to our clinical-stage drug candidates, we are developing a number of IND-enabling drug candidates that we believe have high commercial viability. As of the Latest Practicable Date, we are evaluating three of our IND-filed/IND-enabling candidates' pharmacokinetic and toxicokinetic in a variety of preclinical studies using *in vitro* and *in vivo* laboratory animal testing techniques, and these candidates have shown encouraging preliminary results in our preclinical studies.

IAN0982: IAN0982 is an internally developed multi-specific innate effector activator based on our AIM™ Platform. We are developing IAN0982 as a monotherapy or in combination with other therapeutics including chemotherapy and immunotherapy for the treatment of advanced solid tumors. Our IND application for IAN0982 is expected to be submitted to the NMPA and the FDA in the second quarter of 2024. We maintain the global rights to develop and commercialize IAN0982.

ISH0988: ISH0988 is an internally developed anti-inflammatory and tissue-protective bifunctional fusion protein based on our AIC™ Platform. We are developing ISH0988 as a monotherapy for the treatment of inflammatory bowel disease ("**IBD**"). Our IND application for ISH0988 is expected to be submitted to the NMPA and the FDA in the second quarter of 2024. We maintain the global rights to develop and commercialize ISH0988.

ISH0613: ISH0613 is an internally developed bifunctional antibody fusion protein that simultaneously inhibits B cell activation and IFNα secretion based on our AIC™ Platform. We are developing ISH0613 as a monotherapy for the treatment of SLE. Our IND application for ISH0613 is expected to be submitted to the NMPA and the FDA in the second quarter of 2024. We maintain the global rights to develop and commercialize ISH0613.

COLLABORATION ARRANGEMENT

In 2019, leveraging our platform capabilities and pipeline progress, we planned to further delve into our research and development domain, particularly focusing on simultaneous activation of both the innate and adaptive immune systems. Our initial investigations into the synergistic potential of dual-targeting PD-L1 and CD47 showed promising avenues for exploration. Recognizing that ImmuneOnco Biopharmaceuticals (Shanghai) Inc. ("**ImmuneOnco**") had achieved certain advancements in the differentiated study on SIRP, the ligand of CD47, we were particularly drawn to their drug candidate, namely IBC0966. This PD-L1/SIRPa bifunctional fusion protein matched our envisioned molecular design. With an eye on achieving a more definitive drug profile and capitalizing on the potential synergistic benefits of IBC0966 in tandem with our other pipeline drugs, we initiated a collaboration with ImmuneOnco.

Collaboration Agreement With ImmuneOnco in Relation to the Development of IBC0966

In October 2019, we entered into a collaboration agreement (the "**IBC0966 Agreement**") with ImmuneOnco with respect to the technology transfer, development, manufacture and commercialization of IBC0966. ImmuneOnco is a biotechnology company primarily engaged in the development of immuno-oncology therapies and it is an Independent Third Party to us. For details of IBC0966, see "— Drug Candidates — Clinical-Stage Product IBC0966 (PD-L1/SIRPα antibody fusion protein)" in this section.

Pursuant to the IBC0966 Agreement, ImmuneOnco transferred to us (i) all of its rights and interests, including but not limited to development, manufacture, regulatory filings, and commercialization, in relation to IBC0966 in mainland China, Hong Kong, Macau and Taiwan (the "**Territory**"); (ii) all related patents, if applicable, registered in the Territory; (iii) all technical data and analytical methods relating to the development of IBC0966. Accordingly, ImmuneOnco has transferred to us its invention patent in mainland China in relation to IBC0966 (patent number: CN111278865B), which invention patent covered all the key characteristics of IBC0966, and we have completed the administrative registration of the transfer. The application of this patent was filed on October 24, 2018 and the patent will expire on October 24, 2038.

We are entitled to all rights and interests of IBC0966 in the Territory and continue the development of IBC0966 including, among others, the preclinical and clinical researches, registrational applications, manufacture and commercialization of IBC0966 in the Territory at our costs, while ImmuneOnco retains the rights to develop, register and commercialize IBC0966 outside of the Territory. We do not share any R&D expenses with ImmuneOnco. We will assist ImmuneOnco in submitting IND and NDA applications to regulatory authorities in relation to IBC0966 outside of the Territory. Specifically, we will provide our clinical trial materials in relation to IBC0966 in the Territory, and application materials in relation to chemical, manufacturing and control as well as pre-clinical studies to ImmuneOnco. In return for the aforementioned efforts and assistance that we will make for ImmuneOnco's IND and NDA applications in relation to IBC0966 outside the Territory, as commercially agreed by both parties, we will be entitled to 7.5% of the interests of IBC0966 outside the Territory. In addition, should ImmuneOnco transfer or license its rights of IBC0966 outside of the Territory to a third party, we are entitled to 7.5% of the resulting proceeds garnered by ImmuneOnco.

In exchange of our rights, we are obligated to pay RMB20.0 million assignment fee by installments. As of the Latest Practicable Date, the rights and interests of IBC0966 as well as the related documents and materials had been duly transferred to us and we had paid ImmuneOnco an assignment fee of RMB10.0 million. The remaining RMB10.0 million will be payable upon our obtainment of the marketing approval of IBC0966 from the NMPA. In addition, ImmuneOnco is entitled to low single-digit percentage royalties based on the annual net sales of IBC0966 in the Territory until the earlier of the tenth year after the initial launch of IBC0966 or the expiration of the patents of IBC0966 molecule sequences. As of the Latest Practicable Date, we did not make or owe any royalties to ImmuneOnco.

The IBC0966 Agreement shall remain effective from execution until termination of the agreement. Either party may terminate the IBC0966 Agreement if the other party is in breach of its obligations under this agreement, and fails to take rectification measures after the non-breaching party gives a 30 days' written notice. The IBC0966 Agreement can also be terminated upon mutual consent if IBC0966 fails to obtain IND approval or reach the clinical endpoint due to reasons related to druggability. In addition, in the occurrence of certain safety issues resulting in the failure of IBC0966, we are entitled to a 50% payment return and ImmuneOnco is entitled to restitutions of the transferred rights and interests of IBC0966 upon the termination of the IBC0966 Agreement. The termination of this Agreement shall not release either party from any obligations or liabilities that have arisen under this agreement prior to such termination, nor shall it prevent either party from asserting any rights and remedies that it may have under this agreement or at law.

Apart from the rights and obligations under the IBC0966 Agreement, we procured a limited amount of raw materials (namely, cell culture medium) from ImmuneOnco. Other than the foregoing, there is no past or present relationships or dealings (including family, business, employment, trust, financing or otherwise) between our Group and ImmuneOnco, their respective substantial shareholders, directors or senior management, or any of their respective associates.

RESEARCH AND DEVELOPMENT

We consistently devote resources to research and development to pave for long-term growth. We believe the diversification and expansion of our product pipeline through both in-house research and development and through external collaboration are critical to our long-term competitiveness and success. Our research and development expenses in 2022 and 2023 amounted to RMB53.2 million and RMB43.0 million, respectively.

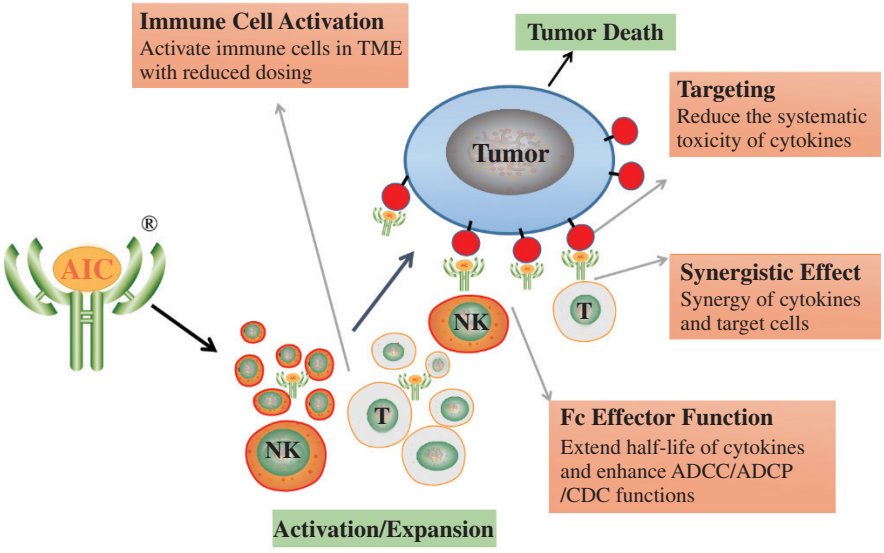
Our fully-integrated biological therapeutic platform encompasses all the key biologic drug development functionalities, and enables us to identify and address potential clinical and manufacturing issues early in the development process so we can direct our efforts towards biologics with the best potential to become clinically active, cost-effective and commercially viable drugs. Our platform spans from the early phase of identifying demand, developing core technologies, managing clinical trials and product registrations, to the manufacturing and marketing of products. We believe that our integrated capabilities give us the agility to formulate our innovation, registration, commercialization and product optimization strategies that can navigate us through rapidly changing market needs, enable us to improve pipeline viability and expedite product development cycle at lower cost.

R&D Platforms

We have built fully-integrated platforms to enable our in-depth R&D in the areas of immunology and oncology. Our core platforms include AIC™ Platform, AEA™ Platform and AIM™ Platform. Our platforms are integrated seamlessly to support key drug development functionalities, including antibody screening, functional evaluation, *in vivo* preclinical studies and biomarker identification. We have the expertise and capability to independently complete the entire drug development process from drug discovery to preclinical research to clinical development and to NDA/BLA application.

Armed ImmunoCytokine Platform, AIC™

Our AIC™ Platform is prominently positioned in the field of immunocytokine development from multiple aspects, including cytokine selection and optimization, antibody selection and engineering, structural design and engineering and production through customized cell line. It is a comprehensive research engine that includes not only a pool of intact IgG antibodies and cytokines, but also functional antibody fragments and other types of immune system modulators. It is able to generate products ranging from immunocytokines to bifunctional fusion proteins. The products designed from the AIC™ Platform may not only include immunostimulants that directly activate both innate and adaptive immunity, but also immunosuppressors that reduce an overactive immune system. Therefore, AIC™ Platform enables us to enrich our pipeline with candidates for treatment of cancer and viral infection, and also candidates for the treatment of autoimmune diseases and emergency care against cytokine storm. Our clinical programs IAP0971, IAE0972 and IBB0979 for cancer immunotherapy, and preclinical programs ISH0988 and ISH0613 for autoimmune diseases were developed based on the AIC™ Platform.



Source: Company data

Our AIC™ Platform successfully addresses technical difficulties for developing immunocytokines. These difficulties range from antibody and cytokine selection and optimization, to final drug production.

- Antibody/cytokine selection. Due to different spatial structure, different types of cytokines behave largely different when fused with antibodies targeting different antigens.

- Structural design. Dose ratio and activity between the selected antibody and cytokine is needed to be balanced to achieve the desired mechanism of actions ("**MoA**") and synergistic effects.

- Manufacturing capabilities. It is challenging for developing and manufacturing immunocytokine molecules, because they are structurally complicated, especially considering the degradation vulnerability of cytokines.

Core competencies of AIC™ Platform include MoA-based antibody-cytokine selection, biology-oriented structural design and protein engineering, and production through customized cell line.

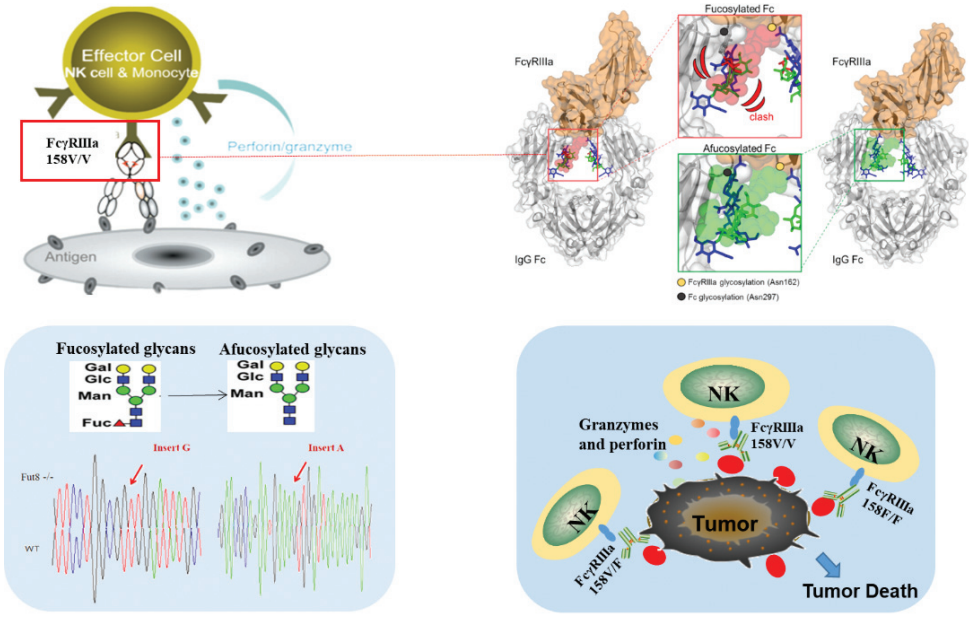
- MoA-based antibody-cytokine selection is the cornerstone to achieve desired synergistic effects between antibody and cytokine. For example, selection of anti-PD-1 antibody and IL-15 cytokine for developing IAP0971 is grounded on their shared action site on the same T/NK cells, leading to great *cis*-synergy. The combination of anti-EGFR antibody and IL-10 is selected based on the potential engager effects it can produce. Specifically, IAE0972 can engage CD8+ T cells through IL-10 while simultaneously targeting tumor cells through the EGFR antibody moiety.

- Structural design and protein engineering module enables us to structurally design and modify our products to achieve improved safety and efficacy profile while reducing manufacturing cost and enhancing product quality manageability. Structural modifications that we are capable to perform through AIC™ Platform include antibody and cytokine engineering, deglycosylation, linker/spacer design and optimization, and tertiary structure alteration. Especially, developed through the AIC™ Platform, IAP0971 employs the natural pairing of IL-15/IL-15Rα, which leads to more efficient dimerization and eliminates the formation of IL-15 homodimer and half antibody fragments. Additionally, a knobs-into-holes structure is introduced in the Fc region of the anti-PD-1 antibody, reducing the mismatch of two different heavy chains. These structural designs result in improved productivity of IAP0971. Furthermore, IAP0971 is also modified by engineering the IL-15/IL-15Rα heterodimers partially embedded into the "hinge" region in the anti-PD-1 antibody. We were the first to design and develop this structure. It can increase the stability of cytokine by "hiding" a substantial portion of cytokine within antibody to protect it from hydrolysis by proteases, as well as balances the activity of cytokine versus antibody by introducing steric hindrance to the cytokine, and in the meantime retains the specificity and affinity of cytokine to bind to its receptor and allows it to mediate immune responses.

- Production through customized cell line is another important function performed by our AIC™ Platform. The cell lines we constructed for producing immunocytokines and other bifunctional fusion proteins are obtained after undergoing multiple rounds of metabolic and growth optimization and are of high expression capacity and excellent purification yield. Coupled with unique cytokine-specific codon optimization, stably expressed vehicles with optimized expression cassettes and our high-throughput screening system, it is able to reach an expression level of 4g/L and one-step affinity chromatography purity of 86%, which is at the top level among rivals both at home and abroad, according to Frost & Sullivan.

ADCC Enhanced Antibody Platform, AEA™

Our AEA™ Platform is a biologically engineered Chinese hamster ovary ("**CHO**") cell line with the FUT8 knocked-out to generate antibodies with enhanced ADCC and improved antitumor activities. Through this bioengineering modification, the CHO cell line will not be able to catalyze the transfer of fucose residue from its donor to its target, and thus is not able to produce any antibody that carries fucose. Because absence of core fucose on the Fc region has been shown to increase the Fc region's binding affinity to its receptor FcγRIIIa present on immune effector cells, fucose-negative antibodies are expected to have enhanced ADCC activities through better activating immune effector cells. Accordingly, AEA™ Platform is expected to produce antibodies with 0% of fucose, which rapidly, stably, and thoroughly enhances the ADCC of antibodies and simplifies the quality control of the products. Therefore, AEA™ Platform can enable us to engineer any antibody or antibody portion (containing a Fc region) of biologics into ADCC enhanced products for enhanced immune effector cells activities.

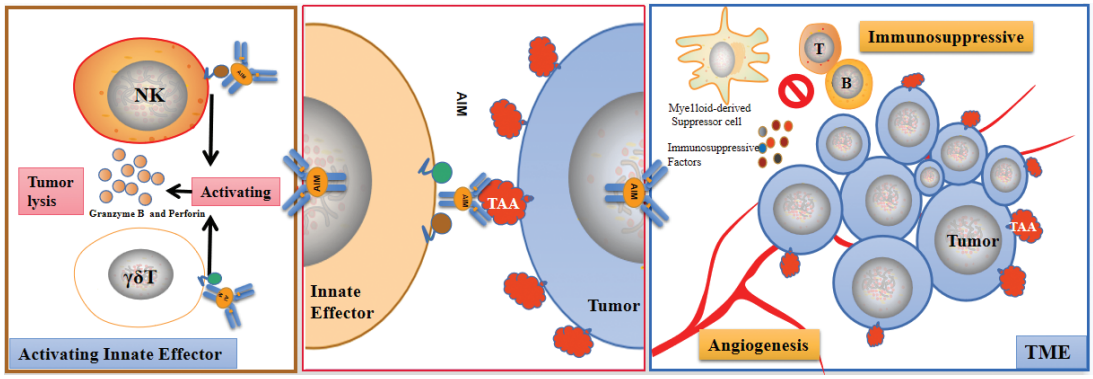


Source: Top left: Kubota et al, Cancer Sci (2009); top right: Yu et al, BioDrugs (2017); bottom left and bottom right: Company data

The feasibility and advantages of AEA™ Platform have been demonstrated by IAH0968, the potential first complete fucose-removal anti-HER2-antibody in clinical stage developed through this platform. We have verified through glycoprotein detection and glycosylation quantification that IAH0968 does not contain any fucose. In addition, *in vitro* and *in vivo* tests showed that the affinity between IAH0968 and its Fc receptor was 10-20 times higher than unmodified or the other ADCC enhanced anti-HER2 antibodies, resulting in greater enhanced ADCC activity and antitumor efficacy.

Armed Innate-effector Multispecific Platform, AIM™

Our AIM™ Platform focuses on designing multi-functional biological products by engaging the innate immune system for cancer immunotherapy. It selects tumor associated antigen antibodies for cancer targeting, receptors agonist antibodies for innate effector activation, and cytokines and other TME factors for immune modulation to design multi-specific antibody fusion proteins, and evaluates them in terms of expression, target binding, *in vitro* and *in vivo* biological activities, as well as druggability. Currently, we have developed several categories of proprietary AIM™ Platform that allow us to explore the combination of innate immunity stimulators with different types and numbers of targets, which provide us with abundant flexibility and diversity of various types of TME modulations for different clinical indications. In other words, AIM™ Platform can design and generate a huge pool of potential product candidates through combinations of different innate immunity stimulators, which will enable us to continuously develop new pipeline products.



Source: Company data

By targeting innate immunity stimulators instead of adaptive immunity stimulators, which is considered more cytotoxic and easily restrained by immune escape of tumors and the immunosuppressive TME, products developed from our AIM™ Platform are expected to achieve desired clinical safety and efficacy profiles. Our preclinical product IAN0982 was developed based on the AIM™ Platform.

R&D Team

Our core R&D team consists of eight members, each with industry experience ranging from over four to 16 years. The expertise of our team members spans the entire spectrum of biopharmaceutical development, encompassing drug discovery, preclinical pharmaceutical research, molecular structural design, drug testing and purification, formulation development, clinical researches, regulatory submissions and platform construction. As of the Latest Practicable Date, we had 43 members in our R&D team. In particular, 29 members focused on Core Products, around 82.8% of whom held master or doctoral degrees in relevant fields.

Our R&D team is led by our executive Director, chief executive officer and chief scientific officer, Dr. YIN Liusong, who had over 16 years of experience in antibody and cytokine development and pipeline management. Dr. Yin published more than 16 research papers in journals indexed in SCI, which were cited by others for more than 500 times. Dr. Yin received his Doctor's degree in biomedical sciences from UMass Chan Medical School. The executive Director and vice president overseeing our R&D is Ms. JIANG Xiaoling. Ms. Jiang had over 15 years' experience in R&D of pharmaceuticals including biosimilar drugs and antibody drugs, and led the development of about 20 innovative biologics and six biosimilars. Ms. Jiang received her master degree in Biochemistry and Molecular Biology from Nanjing University. Members of our experienced in-house R&D team come from a variety of medical backgrounds and has diverse and in-depth knowledge that is critical to strengthening our R&D capabilities.

In addition to Dr. Yin and Ms. Jiang, our core R&D team also consists of six managers with different expertise in drug development. Our pharmaceutical research manager, Mr. WU Chongbing, joined us in 2018 and had over 12 years of experience in protein engineering,

structural design, expression purification, and CMC research. He is responsible for the management of pharmaceutical research of our programs to ensure smooth and on time IND applications. Mr. Wu has contributed to the establishment of several technology platforms, formulation and purification process development, and structural design of antibodies and fusion proteins, and was named as inventor in over 30 patents. Our project evaluation and management manager, Ms. ZHOU Chong, also joined us in 2018 and had over five years of experience in cell line engineering and modification. She is mainly focusing on and responsible for antibody engineering, including cell line construction, antibody glycosylation engineering modification, and multi-specific antibody design. The core members of our R&D team also include our quality and analytic manager Ms. ZHOU Ying, our cell-line and upstream process development manager Ms. ZHU Yanan, our downstream and formulation development manager Mr. GU Haitao, and our *in vitro* pharmacology manager Ms. HUANG Zhenzhen. Leveraging comprehensive expertise of our core R&D team, we have successfully initiated and advanced our Core Products.

Since the inception of our business in 2018, we have been dedicated to the development and construction of R&D platforms facilitating the discovery and development of our pipeline portfolios. Before Dr. Yin and Ms. Jiang joining our Company, the design and establishment of the AIC™ and AIM™ Platforms were primarily led by Mr. Wu, who has completed the preliminary establishment of these two platforms. Leveraging the preliminary model of the AIC™ Platform, Mr. Wu also launched R&D projects for IAP0971 and IAE0972 and led the respective initial molecular structural design. The design and preliminary establishment of the AEA™ Platform were led by Ms. ZHOU Chong, who designed the FUT8 knockout strategy of the AEA™ Platform and verified and constructed cell lines with complete knockout of FUT8. In addition, she launched the R&D project for IAH0968 based on the AEA™ Platform.

Since Dr. Yin joined our Group in November 2020, he has further refined the system for cytokine selection of the AIC™ Platform based on his profound expertise and understanding of mechanisms of action of antibody and cytokines through structural design and activity validation of various immunocytokines. He has also refined the target selection mechanism of the AIM™ Platform to improve the potential efficacy of the generated product candidate leveraging his knowledge of mechanisms of synergistic effects of natural immune cell activators and tumor-associated antigens. Furthermore, he advanced the preclinical research of IAP0971 and IAE0972 by optimizing their respective structural designs, which led to the progression of their clinical process. Specifically, in relation to IAP0971, he proposed that forming a pre-complex of IL-15 with IL-15Rα can effectively avoid the silencing of IL-15 by its receptor in DC cells, placing IL-15/IL-15Rα complex in the middle of the antibody facilitates the regulation of cytokine activity. In relation to IAE0972, he proposed the monovalent design of the EGFR antibody to potentially reduce the skin toxicity of EGFR, and maintaining the natural activity of IL-10 by forming an IL-10 homodimer. Furthermore, he also determines the clinical development strategy of the Core Products based on the mechanism of action of the drug and the competitive landscape of the existing indications, as well as manages and monitors the progress of clinical advancement.

Since Ms. Jiang joined our Group in February 2020, she further refined the AEA™ Platform. Specifically, she led the screening of host cells of the AEA™ Platform to ensure that the growth and metabolism of AEA™ Platform host cells are normal, and verified each cell line through small-scale process studies. She also led the validation of multiple antibody drugs produced by AEA™ Platform host cells to ensure that the expression of the host cells was not affected by biological engineering, and verified the ADCC activity of the antibodies to determine the final cell line of the AEA™ Platform. In addition, Ms. Jiang led the preclinical pharmaceutical research of IAP0971 and IAE0972. She determined the preclinical research protocol in cynomolgus monkeys, and the clinical research protocol for investigating *in vivo* effectiveness and *in vitro* verification of mechanisms of action. Furthermore, she managed the IND applications for IAH0968, IAP0971 and IAE0972.

Drug Discovery and Preclinical Development

Leveraging our proprietary R&D platforms, AIC™, AEA™ and AIM™, we are able to conduct preclinical R&D activities including drug activity screening, studies of cellular functions of drugs, drug biochemical studies and biomolecule detection. The protein structures of our target candidates include single-pass transmembrane proteins, multi-pass transmembrane proteins, structure proteins with dependent molecular partners, and complex glycosylated proteins. Our R&D pathways span protein, whole-cell and Virus-like Particles immunization. We are also fully capable to perform common molecular and cellular biology experimental studies, such as cell activity detection, enzyme-linked immunosorbent assay test, molecular cloning, flow cytometry, and *in vitro* and *in vivo* assays.

- ***Candidate sequence discovery and screening.*** Our new targets are generally screened from candidate sequences via our discovery platforms. We established two discovery platforms – a mouse hybridoma platform for the production of full-length antibodies and a camelid antibody phage display screening platform for the production of nanobodies, enabling the construction of multi-target antibodies.

- ***Infrastructure in support of discovery platforms.*** Our discovery platforms are equipped with comprehensive infrastructure, including a hybridoma cell culture room for culture and fusion of myeloma and hybridoma cells; a physicochemical laboratory for screening of protein and cell binding; and a cell culture room for culture of tumor cells and function cells for *in vitro* activity evaluation.

- ***Evaluating functions and biological activities of candidate sequences.*** We will further evaluate the functions and biological activities of the selected antibody candidates. Early in the phase of candidate discovery and screening, we have established customized methods to evaluate the target binding affinity, competitive inhibition activities and biological functions of the candidate antibodies, by means of which we determine the candidate sequences with *in vitro* functionality.

- ***Evaluating in vivo efficacy and metabolism of rodents.*** We further evaluate the *in vivo* efficacy of molecules via the tumor or autoimmune disease models on laboratory rodents. Based on the results of efficacy test, we pick two to three molecules with clinical potential for further research on *in vivo* metabolism in rodents.

- ***Humanization and protein engineering.*** We pick the optimal germline from various forms of antibodies and transplant the complementarity-determining region of the non-humanized antibody to the humanized framework, followed by a restoration mutation to ensure the antibody affinity. Then we enhance druggability of the target antibodies by the post-translational modification in proteins.

With our preclinical research capability and leveraging our R&D platforms, we can efficiently complete target determination, screening optimization and IND application so as to continuously enrich our pipeline portfolio. We have the experience and ability to independently complete the entire drug development process from drug discovery to preclinical research to clinical development and to NDA/BLA application.

Clinical Development

Clinical Trial Design and Implementation

Our medical and clinical development team coordinates our trial design and execution, and manages the procedures of our clinical trials with the assistance of CROs, including implementation, drug supply, collection and analysis of trial data, and preparation of trial reports. Our trial advancements are driven by our clinical development experience, well-designed trial protocols, multi-center trial strategy in close collaboration with PIs, and efficient trial execution. We employ a clinical-demand-oriented approach to our R&D efforts. We strategically design the clinical trials of our drug candidates, critically select the registration pathways, diligently conduct our clinical trials to ensure speed of execution and data quality, and maintain constructive dialogues with the regulatory authorities to achieve optimal clinical efficacy, and accelerate the approval process of our drug candidates.

Our team is also responsible for the selection of trial sites. We select trial sites based on multiple factors. We regularly communicate with collaborating hospitals and principal investigators that can support our clinical trials of different indications at different stages. We believe that the size and the geographic diversity of these institutions provide us with a significant advantage in implementing large-scale clinical trials and also enable us to conduct multiple clinical trials concurrently.

Collaboration With CROs and Contract Service Providers

We take the lead in preclinical research, and design the clinical trials and protocols by ourselves. In line with the practice in the pharmaceutical industry, we engage CROs and third-party contract service providers to conduct and support our preclinical studies and clinical trials. They primarily assist in our research and development efforts by performing a

range of supportive tasks, such as toxicological testing, drug metabolism and pharmacokinetics ("**DMPK**") studies, early exploration of pipeline potential and site oversight, thereby enhancing the efficiency and effectiveness of our research initiatives. We closely supervise the activities of these third-party collaborators. We monitor their work progress to ensure they perform their duties to a standard in line with our protocols and industry benchmark to safeguard the integrity of the data collected from the trials and studies.

We engage the CROs and other contract service providers and research centers in our clinical trials on a project-by-project basis. We have taken several initiatives to make sure that these institutions perform their duties in a manner that complies with our protocols and applicable laws and to protect the integrity of clinical data. We provide these institutions with the final clinical trial protocols and a series of trainings to ensure their familiarity with the trials. They conduct the clinical trials based on our protocols, and we designate internal personnel to supervise the implementation phase. The following table sets forth the detailed information of the key contract service providers engaged by us during the Track Record Period:

Identity	**Background**	**Primary Involvement**	**Our purchase amount during the Track Record Period** *(RMB'000)*
CRO A	a pharmaceutical preclinical integrated R&D service CRO located in Shanghai, which mainly engaged in preclinical pharmacokinetics and safety evaluation research	Toxicological testing and DMPK evaluation	13,822
CRO B	a company based in Shanghai, which principally engaged in technology development, technology consulting, and clinical trial data management and statistical analysis services	Clinical data management	2,175
CRO C	a biotechnology company based in Suzhou, which mainly engaged in CRO services	Contract research services and testing	1,038

Identity	Background	Primary Involvement	Our purchase amount during the Track Record Period *(RMB'000)*
CRO D	a CRO company based in Nanjing, which mainly engaged in research and technology development relating to pharmaceutical and biological products	Sample testing	1,711
CRO E	a pharmaceutical company based in Guangzhou, which mainly engaged in CRO and CDMO services	Cell banking and testing, virus clearance validation	2,538
			21,284

Below is a summary of the key terms of an agreement we typically enter into with our CROs or contract service providers:

- ***Services.*** Our cooperating partner provides the research and development and technical services required by us, including but not limited to the implementation and management of a preclinical or clinical research project, preclinical safety evaluation, PK/PD research and clinical sample testing, as specified in the agreement.

- ***Term.*** Our cooperating partner is required to perform its services and complete the preclinical or clinical research project within the prescribed time limit set out in each agreement, or until the agreement is terminated by mutual agreement, by prior written notices from either party, or due to a material breach as stipulated in the agreement.

- ***Payments.*** We are required to make payments to our cooperating partner in accordance with the payment schedule agreed by the parties.

- ***Intellectual property rights.*** We own all intellectual property rights arising from the preclinical or clinical research project.

- ***Confidentiality.*** Our cooperating partner is obligated to keep confidential all the data, information or contents we distributed to our cooperating partner related to the project specified in the agreement, and such obligation may survive the termination of the agreement.

- ***Risk allocation.*** The risk allocation between the parties and indemnification are subject to further negotiation between the parties.

We determine the service fee with our contract service providers based on the expected or actual work performed by them as well as the estimated or actual cost incurred by project basis. During the Track Record Period, none of our CROs or other contract service providers, including their directors, shareholders and senior management, had any past or present relationship with us or our subsidiaries, shareholders, directors or senior management, or any of their close associates.

We believe working with CROs and contract service providers shortens the time required for drug development by generating the requisite data reliably and efficiently.

CMC AND MANUFACTURING

Chemistry, Manufacture & Controls ("CMC") Team

Our CMC team provides strong support throughout the drug development process. Our CMC team is led by Mr. JIANG Dongcheng, the vice president and head of production, who had 10 years of experience in GMP manufacturing. Our CMC team is mainly responsible for cell line development, upstream and downstream process development, formulation development, GMP-compliant manufacturing and quality management.

Manufacturing Facilities

We have established our own global GMP-compliant manufacturing facilities in Nanjing, PRC, which meet both clinical and commercial production demands for quantity, quality and dosage form of our drug candidates. We currently have four active drug substance production lines up to a total capacity of 1,600L, including three 200L and one 1,000L disposable bioreactors. We have successfully completed over 30 production batches of immunocytokines, mAbs, bsAbs and fusion proteins, which fulfilled the needs for preclinical studies, pilot production of antibody drugs and early phase clinical trials. In addition, we have completed the installation of a production line for 5,000L bioreactor capacity, and completed the qualification in November 2023. When putting into operation, it will enable us to manufacture our drug candidates for Phase III clinical trials and commercialization in-house. Our drug product facilities include one commercial-scale liquid injection filing production line and one commercial scale lyophlized powder production line, which enables us to prepare biological products into various dosage forms. Leveraging the vast experience of our industry veterans in manufacture of pharmaceutical products, we strategically front-loaded our production capacity

infrastructure in a relatively cost-efficient manner. As compared with production outsourcing, our robust independent production capability guarantees a stable and sufficient supply of drug candidates with more manageable production costs and guaranteed quality.

The table below sets for the production details of our pipeline products as of the Latest Practicable Date:

Pipeline product	Dosage form	Total volume produced as of the Latest Practicable Date	Number of batches produced for clinical use	Number of batches produced for non-clinical use	Success rate of product release
IAH0968	lyophilized powder	1,200L	3	3	100%
IAP0971	lyophilized powder	600L	1	2	100%
IAE0972	lyophilized powder	800L	2	2	100%
IBB0979	lyophilized powder	400L	1	1	100%
IBC0966	lyophilized powder	800L	2	2	100%
IBD0333	lyophilized powder	400L	1	1	100%

Leveraging our manufacturing capacities, we occasionally provided contract manufacturing services, primarily including cell line development process development, GMP/cGMP production, sample detection and stability study. We monitor and measure our CMC process and ensure sufficient manufacturing capacity in support of clinical trials. During the Track Record Period, we provided contract manufacturing services to one biotechnology company based in Hefei, Anhui Province, for production of monoclonal antibody drug in compliance with GMP/cGMP standards. The contract manufacturing services agreement set forth the exact scope of services with detailed specifications, standards, requirements and timeline for each type of services. The service fees were determined mainly based on the amount and type of services we provide and the cost of raw materials and consumables. For details, see "Financial Information — Description of Major Components of Our Results of Operations – Other Income" in this document. We expect to devote our productive forces to our own drug candidates and products as our clinical trials progress and after our commencement of commercialization. This biotechnology company is an Independent Third Party. None of our Directors, their close associates or any shareholder who, to the knowledge of our Directors, owned more than 5% of our issued share capital as of the Latest Practicable Date, had any interest in this biotechnology company during the Track Record Period.

CMC

CMC Activities and Capabilities

CMC refers to activities to properly define methods for manufacturing processes, product characteristics and testing, product storage and release to clinical usage in order to ensure that a pharmaceutical product is safe, effective and consistent between batches. Because of the complexity of therapeutic antibody, CMC is essential for antibody drug development from cell line development to process development to formulation.

Our CMC platform, which includes our proprietary manufacturing processes and related analytics, contributes to the potency and the safety profile of our product candidates. We endeavor to build our CMC expertise and create proprietary end-to-end manufacturing process with the capability to produce high quality, generally well-tolerated and potent product candidates. We believe that the combination of processes, analytics, know-how and understanding of biological immunotherapies that forms our CMC capability is competitive in the industry. Our proprietary process is made possible through a set of key in-house capabilities, ranging from process development to analytical capabilities, manufacturing, quality control and quality assurance. The modularity of our platforms and product characterization enable us to effectively leverage the knowledge we gained from our existing programs to optimize the development of new programs.

Cell Line Development

Our manufacturing process commences with cell-line development. In this stage, leveraging our R&D platforms, we utilize advanced biological engineering techniques to create cell lines, such as CHO and FUT8-knockout cell lines, that are capable of producing the desired therapeutic proteins. Theses cell lines, once established, served as the foundation for our production process.

Process Development

The process development can be generally divided into the upstream and downstream process development. Built on our advanced platform technologies, our process development capability ensures the biologics delivery for our preclinical studies and clinical trials:

- *Upstream process development*. The upstream process development, including, among others, cell thawing, cell proliferation, media optimization and focuses on generating products with a high product titer, high productivity and high quality.

- *Downstream process development*. The downstream process development improves the purity of biologics and assures safety through various chromatographic and non-chromatographic technologies to improve the efficiency of purification.

Formulation Development

Diving into researches on stability of antibody proteins, the osmotic regulation process, the protein structure and surface tension and other aspects in the process of drug formulation, we have established expertise in the development of drug formulations and conducted over ten formulation studies for different antibody proteins. Meanwhile, we have established production lines spanning lyophilization, vial filling and prefilled syringe. Through the formulation screening and optimization, our liquid filing capacity is up to 150 vials/minute while our lyophilization product filling capacity can reach 40,000 vials/batch.

We determine the optimal dosage form based on the mechanism of action and anticipated clinical use of various drug candidates. The table below sets forth a general timeline for the determination and development of dosage forms:

Development Phase	Key Steps	Approximately Time Consumed
Drug candidate characterization	Preliminary selection between the dosage forms of liquid injection and lyophilized powders	Four weeks
Cell line construction	Preliminary screening of formulation and preparation technique	Eight weeks
Laboratory development	Verification of prescription and development of formulation process	Eight weeks
Pilot scale production	Confirmation of prescription and formulation process	Four weeks
Early clinical research	Further development of the formulation in terms of dosage form, concentration, prescription, and specifications	One to two years
Pivotal clinical research	Finalization of the formulation's dosage form, concentration, and prescription	Two to three years

GMP-Compliant Manufacturing

We have our own global GMP-compliant manufacturing facilities and strictly implemented the requirements under the GMP/cGMP standards, Chinese and U.S. pharmacopoeias and other relevant regulations and guidelines in our product manufacturing process. We have completed the installation of a production line for 5,000L bioreactor capacity, and completed the qualification in November 2023. When putting into operation, it will enable us to manufacture our drug candidates for Phase III clinical trials and commercialization in-house. Our manufacturing capabilities play a critical role in our drug research and development and pave the way for our future commercialization.

Quality Management

Quality control ("**QC**") and quality assurance ("**QA**") are crucial to us. We endeavor to ensure the quality of our operation through a comprehensive quality management system in accordance with the regulations of the NMPA and the FDA and other applicable regulations, including GMP/cGMP and the standards of the Chinese and American Pharmacopoeias.

We have established QC and QA procedures for monitoring operations to ensure that they meet relevant regulatory and internal quality requirements. We implement QC measures for the development and production process, mainly including control and inspection of raw materials, management of each step of the development and production procedures, inspection of samples, establishment of internationalized product release standards, and risks evaluation during the product development and manufacturing.

Quality Control: Our QC team is mainly responsible for quality inspection of GMP-compliant manufacturing, analytical method validation, product quality standard establishment, product release testing, and stability assessment. Our QC team also inspects raw materials, intermediate products, raw liquids, finished products, and decides whether to release such materials for manufacturing. Process validation is generally conducted after the initiation of the pivotal clinical stage, and the key steps primarily include (i) the finalization of process validation plan that takes approximately one month; (ii) the preparation of materials for validation that takes approximately one month, and (iii) the validation process for three batches of drug substance and drug product that takes approximately four months. The analytical method validation for the BLA applications is typically conducted with the first batch of drug substance from the process validation and the whole process usually takes around two to four months.

Quality Assurance: Our QA team is mainly responsible for managing experimental documents, overseeing manufacturing site and final products for clinical usage, compliance assessment, and the inspection and audit of our outsourced vendors. We implement strict procedures for receiving and releasing of the raw materials used in the production, intermediate products, raw liquids and buffers, and finished products.

We have established a series of internal procedures and protocols including standard operating procedures for quality management of manufacturing process, product release and stability study. We also have standard operating procedures in place to ensure that the finished production meets the process requirements by relevant regulatory authorities. Such procedures ensure the high quality of our products used for clinical trials. In general, the Center for Food and Drug Inspection of NMPA will conduct the on-site GMP compliance inspection at the time when we submit BLA applications for our product candidates, or it may choose to conduct spot checks after the launch of products. We anticipate to receive the GMP compliance inspection when we submit BLA applications for our product candidates. As of the Latest Practicable Date, no deficiencies had been found in relation to our manufacturing process.

Inventory Management

Our inventories consist of raw materials and consumables for production of drug substance. As of December 31, 2022 and 2023, we had inventories of RMB0.9 million and RMB0.8 million, respectively. We generally maintain an inventory level for raw materials to support our preclinical and clinical demands based on the research and development plans for our drug discovery and pipeline product candidates. To ensure the quality of our inventory and prevent inventory loss due to improper storage, we conduct periodic inspections of our warehouses, ensuring that our inventories are stocked in appropriate conditions and are able to meet the needs of our operations.

Regulatory Affairs

Our regulatory affairs team is responsible for the registration filings and management of intellectual properties for our product candidates. To ensure the compliance with the application and registration requirements in relation to clinical trials and commercialization, our regulatory affairs team is responsible for assembling application dossiers for IND and NDA/BLA, addressing inquiries from relevant authorities, conducting CMC and cGMP compliance assessments for product candidates to ensure their compliance with relevant regulations. We possess both knowledge and experience with regard to regulatory filings in China and the U.S.

COMMERCIALIZATION

We currently have no drug approved or in commercial stage yet. However, we have been building up our commercial planning and portfolio management capability since our pipeline drug candidates entered into clinical trials. When the drug candidates are in late-stage development and getting closer to NDA or BLA filing, we intend to form our in-house marketing and sales team by recruiting senior-level sales and marketing personnel who are experienced in treatment fields we focus on. Our marketing and sales team will be responsible for market strategy, product positioning, market access, market penetration, promotion activities, and patient support. They will help oncologists, immunologist and other relevant industry experts understand the MoA, clinical data and differentiation of our products. We will promote medical science liaisons including KOL engagement, medical education, medical conference management, investigator-initiated study support, and promote product differentiation. We may also seek strategic collaboration opportunities for the commercialization of our drug candidates in China. In particular, we may selectively license-out, establish joint ventures or through other forms of partnerships collaborate with leading biopharmaceutical companies for executing late-stage clinical trials and/or marketing our drug candidates.

Pricing

When our Core Products and our other product candidates progress to commercialization, we mainly will determine their prices based on a number of factors, including our costs of production, prices of competing drugs (if applicable), differences in features between our drugs and competing drugs, health economics, market trends and changes in the levels of supply and demand. Considering that some cancer patients, especially late-stage cancer patients, may be reluctant to pay for highly-priced drugs to treat terminal or deadly diseases, in addition to aforementioned main factors, we may also consider treatment needs and payment preference of late-stage cancer patients when determine the prices. We plan to make a detailed pricing strategy when such drug candidates progress toward commercialization.

As of the Latest Practicable Date, there was no pricing guidance or centralized procurement requirement set by the PRC government on our product candidates. In order to gain market share against existing and future branded and generic competitors, we will seek inclusion of our Core Products and other product candidates into the NRDL and other reimbursement programs through active negotiations with the relevant authorities such inclusion. However, inclusion into the NRDL is evaluated and determined by the relevant government authorities and we may face significant competition for successful inclusion.

SUPPLIERS AND RAW MATERIALS

Suppliers

During the Track Record Period, our purchases mainly include contract services in support of our preclinical and clinical research, premise leases and equipment procurement, and application fees relating to the regulatory filings and clinical trial applications. In terms of our purchases of CRO services and other contract research services, we are generally required to make payments upon achieving certain milestones as stipulated in the related agreements.

The following table sets forth details of our five largest suppliers in 2023:

Five largest suppliers	Commencement of business relationship	Background	Major purchases	Credit terms	Purchase amount	Percentage of total purchase
					(RMB'000)	*(%)*
Supplier A	2021	a pharmaceutical preclinical integrated R&D service CRO located in Shanghai, which mainly engaged in preclinical pharmacokinetics and safety evaluation research	Contract research services and testing	Instalment payments to be made upon completion of milestones, as applicable	2,729	12.0
Supplier B	2022	a pharmaceutical company based in Guangzhou, which mainly engaged in CRO and CDMO services	Contract research services and testing	Instalment payments to be made upon completion of milestones, as applicable	2,538	11.2
Nanjing Bode	2018	a company based in Nanjing, which principally engaged in R&D, manufacturing and sales of small molecule active pharmaceutical ingredients	Premise lease	payment before next lease term	2,433	10.7
Supplier C	2022	a clinical trial site based in Jinan, providing clinical trials related services	Clinical trials	Instalment payments to be made upon completion of milestones, as applicable	1,964	8.6
Supplier D	2011	a company based in Shanghai, which principally engaged in clinical stage CRO services	Contract research services	Instalment payments to be made upon completion of milestones, as applicable	1,674	7.4
Total					**11,338**	**49.9**

The following table sets forth details of our five largest suppliers in 2022:

Five largest suppliers	Commencement of business relationship	Background	Major purchases	Credit terms	Purchase amount	Percentage of total purchase
					(RMB'000)	*(%)*
Supplier A	2021	a pharmaceutical preclinical integrated R&D service CRO located in Shanghai, which mainly engaged in preclinical pharmacokinetics and safety evaluation research	Contract research services and testing	Instalment payments to be made upon completion of milestones, as applicable	11,093	35.2
Nanjing Bode	2018	a company based in Nanjing, which principally engaged in R&D, manufacturing and sales of small molecule active pharmaceutical ingredients	Premise lease	payment before next lease term	2,224	7.1
Supplier E	2020	a medical and food engineering company based in Shanghai, which mainly engaged in research, development, manufacture and sales of medical equipment	Equipment purchase	Instalment payments within 12 months after acceptance of goods	1,679	5.3
Supplier F	2021	a biotechnology company based in Suzhou, which mainly engaged in testing services	Contract research services and testing	Instalment payments to be made upon completion of milestones, as applicable	1,038	3.3
NMPA	2020	the National Medical Products Administration responsible for registration of medical devices for the Chinese market	Clinical trials application	15 days after acceptance of application	1,008	3.2
Total					**17,042**	**54.1**

In 2022 and 2023, the aggregate purchase attributable to our five largest suppliers in each year accounted for 54.1% and 49.9% of our total purchases, respectively. The purchase attributable to our single largest supplier in each year accounted for 35.2% and 12.0% of our total purchases, respectively. We believe that adequate alternative sources for such supplies exist and we will establish necessary relationships with alternative sources based on supply continuity risk assessment.

To the best of our knowledge, all of our five largest suppliers in each year during the Track Record Period were Independent Third Parties, except for Nanjing Bode Biological Pharmaceutical Co., Ltd. (南京博德生物製藥有限公司) ("**Nanjing Bode**") which was a related party to us during the Track Record Period but has become an Independent Third Party since July 2023. For further details, see "Relationship with Our Controlling Shareholders — Clear Delineation of Business — Nanjing Bode" in this document.

During the Track Record Period, we leased premises and purchased equipment from Nanjing Bode, which was on an arm's length basis and in the ordinary course of our business operation. During the initial stage of production line setup, we opted to lease premise and purchase equipment from Nanjing Bode as it had leasable properties and ready-to-use machinery equipment with proven quality that met our specific manufacturing needs. Such arrangement facilitated a swift and efficient deployment of our manufacturing facilities. We believe that there is no concentration risk relating to our transactions with Nanjing Bode as (i) there are plenty of alternative locations with valid titles for us to choose from and we do not foresee difficulties or administration burden to relocate if needed; and (ii) the purchase of machinery and equipment was non-recurring in nature. We did not purchase any other machinery and equipment from Nanjing Bode during the Track Record Period and up to the Latest Practicable Date.

During the Track Record Period, we purchased a large portion of the contract research services and testing services from certain CROs. We select our CRO collaborators and third-party service providers based on various factors, including but not limited to their quality standard, regulatory compliance, technical expertise, production capacity, geographic proximity, track record and reputation in the industry, and reliability in meeting delivery timelines. For details of our collaboration, see "— Research and Development — Clinical Development — Collaboration with CROs and Contract Service Providers" in this section. We consider it important to maintain good business relationships with CROs and our other suppliers and where possible, diversify our supplier base so as to avoid any disruptions in service supply. Our Directors confirm that during the Track Record Period and as at the Latest Practicable Date: (i) we did not experience any material difficulties in obtaining clinical services in a timely manner; (ii) we did not have any material disputes with our major suppliers; (iii) as confirmed by F&S, there are many qualified service providers which are experienced in the area we focused on; and (iv) as our clinical trials needs expanded with the development of our product candidates as more of them entered into clinical trials and for indications expansion, we plan to collaborate with more service providers to support us.

Raw Materials

During the Track Record Period, we have procured raw materials and consumables for the production of our drug candidates and our contract manufacturing services. During the Track Record Period, we did not experience any significant fluctuations in raw material prices or delays that had a material impact on our results of operations or financial position. The raw materials for our drug candidates to be used in clinical trials as well as materials for our laboratory use are generally readily available in the market through multiple suppliers.

INTELLECTUAL PROPERTY

Intellectual property, including patents, trade secrets, trademarks and copyrights, is critical to our business. Our success depends in part on our ability to obtain and maintain intellectual property protection for our drug candidates, novel discoveries, product development technologies, inventions and know-how. Our success also depends in part on our ability to defend and enforce our patents including patents that we have or may issue from our patent applications, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of other parties.

We have adopted a strategy to develop a global portfolio of patents to protect our drug candidates and product development technologies. As of the Latest Practicable Date, we owned 14 issued patents and 124 patent applications, including 54 patent applications in China, nine patent applications in the U.S., and 61 patent applications under the Patent Cooperation Treaty ("**PCT**"), relating to certain of our drug candidates and product development technologies.

As of the Latest Practicable Date, (i) for our Core Product IAH0968, we had three material patents granted in China, and three material patent applications in China, and two material patent applications under PCT; (ii) for our Core Product IAP0971, we had one material patent granted in China, five material patent applications in China, and one material patent application in the U.S.; and (iii) for our Core Product IAE0972, we had five material patent applications in China and one material patent application under PCT. The following table summarizes the details of the material patents by our Company in connection with our Core Products:

Core Products	Patent/Patent application No.	Protection Scope	Jurisdiction	Status	Date of Application	Date of Grant	Date of Expiration	Commercial Rights	Applicant	Inventors
IAH0968	202110589738.6	A CHO cell culture method	PRC	Granted	2021/05/28	2023/10/24	2041/05/28	proprietary rights	SunHo (China) BioPharmaceutical	ZHU Yanan, JIANG Xiaoling, CHEN Jun, DING Liangliang

Core Products	Patent/Patent application No.	Protection Scope	Jurisdiction	Status	Date of Application	Date of Grant	Date of Expiration	Commercial Rights	Applicant	Inventors
IAH0968	202110520687.1	A CHO cell culture method	PRC	Granted	2021/5/13	2024/1/12	2041/5/13	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, ZHU Yanan, WANG Xiuyuan[3]
IAH0968	202011532430.X	Fucose removed anti-HER2 antibody freeze-dried powder injection and preparation method thereof	PRC	Granted	2020/12/23	2024/1/2	2040/12/23	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, WU Chongbing
IAP0971	202010534034.4	A multifunctional antibody, its preparation and application thereof	PRC	Granted	2020/06/12	2023/03/21	2040/06/12	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling[2], JIANG Dongcheng, WU Chongbing

The following table summarizes the details of the material filed patent applications by our Company in connection with our Core Products:

Core Products	Patent/Patent application No.	Protection Scope	Jurisdiction	Status	Date of Application	Commercial Rights	Applicant	Inventors[1]
IAH0968	202310193170.5	Use of an anti-HER2 antibody in the preparation of drugs for the treatment of cancer	PRC	Pending	2023/03/03	proprietary rights	SunHo (China) BioPharmaceutical	YIN Liusong, JIANG Xiaoling, XU Tie
	202310193224.8	Use of an anti-HER2 antibody in the preparation of drugs for the treatment of cancer	PRC	Pending	2023/03/03	proprietary rights	SunHo (China) BioPharmaceutical	YIN Liusong, JIANG Xiaoling, XU Tie
	202011244613.1	A method of knocking out the FUT8 gene	PRC	Pending	2020/11/10	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, ZHOU Chong, WU Chongbing
	PCT/CN2024/079489	The usage of an anti-HER2 antibody in the preparation of cancer therapeutic drugs	PRC	Pending	2024/03/01	Proprietary rights	SunHo (China) BioPharmaceutical	YIN Liusong, JIANG Xiaoling, XU Tie

Core Products	Patent/Patent application No.	Protection Scope	Jurisdiction	Status	Date of Application	Commercial Rights	Applicant	Inventors[1]
	PCT/CN2024/079492	The usage of an anti-HER2 antibody in the preparation of cancer therapeutic drugs	PRC	Pending	2024/03/01	Proprietary rights	SunHo (China) BioPharmaceutical	YIN Liusong, JIANG Xiaoling, XU Tie
IAP0971	US17/633,477	A multifunctional antibody, its preparation and application thereof	U.S.	Pending	2020/07/09	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling[2], JIANG Dongcheng, WU Chongbing
	202310171538.8	A multifunctional antibody, its preparation and application thereof	PRC	Pending	2020/06/12	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling[2], JIANG Dongcheng, WU Chongbing
	202110010966.3	A target PD-1 multi-functional antibody combination	PRC	Pending	2021/01/06	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, WU Chongbing, ZHU Cailin, DU Wuchen[3]
	202110010974.8	A multi-functional antibody combination	PRC	Pending	2021/01/06	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, WU Chongbing, ZHU Cailin, DU Wuchen[3]
	202110329842.1	A fusion protein sample fast analysis method	PRC	Pending	2021/03/29	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, ZHOU Ying, WU Huimin, LIU Mengting[3]
	202211293585.1	A fusion protein purification method	PRC	Pending	2022/10/21	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, WU Chongbing, GU Haitao

Core Products	Patent/Patent application No.	Protection Scope	Jurisdiction	Status	Date of Application	Commercial Rights	Applicant	Inventors[1]
IAE0972	202110141918.8	A stable anti-EGFR antibody mixture	PRC	Pending	2021/02/02	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, WU Chongbing, ZHU Cailin, DU Wuchen[3]
	202110497420.5	Anti-EGFR fusion protein or combination of its antigen-binding fragments and application thereof	PRC	Pending	2021/05/08	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, WU Chongbing, ZHOU Ying, DU Wuchen[3]
	202110264314.2	A fusion protein fast analysis method	PRC	Pending	2021/03/11	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, WU Chongbing, ZHOU Ying, WU Huimin, LIU Mengting[3]
	202210424493.6	An asymmetric fusion protein purification method	PRC	Pending	2022/04/21	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, YIN Liusong, WU Chongbing, GU Haitao
	202211220978.X	A fusion protein purification method	PRC	Pending	2022/10/08	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, YIN Liusong, GU Haitao
	PCT/CN2023/123701	A heterodimeric fusion protein and application thereof	PCT	Pending	2023/10/10	proprietary rights	SunHo (China) BioPharmaceutical	JIANG Xiaoling, YIN Liusong, WU Chongbing

Notes:

(1) All inventors of our material patents and patent applications are our current or previous R&D personnels.

(2) With JIANG Xiaoling's knowledge in the field of biotechnology, biochemistry, cell line construction and biosimilar drugs through her academic studies and past working experience, JIANG Xiaoling participated in discussions with, among others, WU Chongbing for the R&D project for IAP0971 at its initial phase and provided suggestions on IAP0971's certain features such as expression and purification outside her working hours during the time when her employment was with Nanjing Yoko Pharma Co., Ltd. (南京優科製藥有限公司) (a wholly-owned subsidiary of Nanjing Yoko). To recognize her contribution to and participation in the R&D project for IAP0971, JIANG Xiaoling was also named as one of the inventors in respect of a patent application of our Group numbered 201910776848.6 (the "**Patent Application**") which subsequently became a priority right for another patent of our Group numbered 202010534034.4 and two other patent applications of our Group numbered 202310171538.8 and US17/633,477, respectively. As confirmed by Nanjing Yoko, Ms. Jiang did not make use of any resources and technology of Nanjing Yoko in connection with her such participation and the Patent Application is not a service invention (職務發明創造) in which Nanjing Yoko has had any interest. Further, as advised by the Company's legal advisers as to intellectual property laws, Jingtian & Gongcheng and Venture Partner, LLC, the risk of disputes arising from the ownership of the Patent Application is relatively remote.

(3) Our previous employees.

As of the Latest Practicable Date, we had three material patent applications in the U.S., three material patent applications in China for AIM™ Platform, four material patent applications in China, and one material patent application under PCT for AIC™ Platform, and one material patent application in China for AEA™ Platform. The following table summarizes the details of the material filed patent applications by our Company in connection with our R&D platforms:

Platform/ product candidates	Patent/Patent application No.	Protection Scope	Jurisdiction	Status	Date of Application	Commercial Rights	Applicant	Inventors[1]
AIM™	US18/569,320	A multi-specific antigen-binding protein and use thereof	U.S.	Pending	2022/06/13	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling
	US18/293,500	A multi-specific antigen-binding protein and use thereof	U.S.	Pending	2022/07/27	Proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling
	US18/293,515	A multi-specific antigen-binding protein and use thereof	U.S.	Pending	2022/07/27	Proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling
	202280052098.8	A multi-specific antigen-binding protein and its application	PRC	Pending	2022/06/13	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling
	202280052163.7	A multi-specific antigen-binding protein and its application	PRC	Pending	2022/07/27	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling
	202280052131.7	A multi-specific antigen-binding protein and its application	PRC	Pending	2022/07/27	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling

Platform/ product candidates	Patent/Patent application No.	Protection Scope	Jurisdiction	Status	Date of Application	Commercial Rights	Applicant	Inventors[1]
AIC™	202110972207.50	A multifunctional fusion protein and application thereof	PRC	Pending	2021/08/24	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, WU Chongbing, YIN Liusong, JIANG Xiaoling, WANG Yizhen[2]
	202110971791.20	A multifunctional fusion protein and application thereof	PRC	Pending	2021/08/24	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, WU Chongbing, YIN Liusong, JIANG Xiaoling, WANG Yizhen[2]
	202210801304.20	A dimeric fusion protein and applications thereof	PRC	Pending	2022/07/08	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling
	202210853460.30	A dimeric fusion protein and applications thereof	PRC	Pending	2022/07/08	proprietary rights	SunHo (China) BioPharmaceutical	WU Chongbing, YIN Liusong, JIANG Xiaoling
	PCT/CN2023/105535	A heterodimeric fusion protein and its application	PCT	Pending	2023/07/3	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling
AEA™	202110752316.60	A method for knocking out the FUT8 and the antibodies obtained thereof	PRC	Pending	2021/07/02	proprietary rights	SunHo (China) BioPharmaceutical	ZHOU Chong, YIN Liusong, JIANG Xiaoling

Notes:

(1) All inventors of our material patents and patent applications are our current or previous R&D personnels.

(2) Our previous employees.

Our IAH0968 is featured by completely defucosylated anti-HER2 antibody and indication, which have been covered by patent No. CN202110589738.6 and patent applications No. CN 202310193170.5, CN 202310193224.8.

Our IAP0971 is featured with two main components. Each component consists of a paired heavy and light chain. These pairs are designed to bind to the PD-1 antigen, a key target of the immunotherapy. Additionally, one heavy chain in our product comprises a cytokine IL-15 moiety and an immunoglobulin Fc part, while the other comprises a cytokine IL-15 receptor and an immunoglobulin Fc part. These elements are designed to interact with each other, enhancing the product's functionality. The features of IAP0971 have been covered by patent No. CN 112409484B and patent applications No. CN 202310171538.8 and US 17/633,477.

Our IAE0972 is featured by a composition of a first heavy chain, a light chain, and a second heavy chain. The first heavy chain features an Fc region fused with IL10. In contrast, the second heavy chain collaborates with the light chain to create a targeted portion specifically binding to EGFR. Together, these chains synergize to form the heterodimer fusion protein. The features of IAE0972 have been covered by patent application No. PCT/CN2023/123701.

In view of the above, we come to the conclusion that our current patents and patent applications have covered all the key features or characteristics of the Core Products.

We do not foresee difficulties in obtaining the relevant approvals of patent applications that cover the key features or characteristics of our Core Products based on a comprehensive review of the following facts. Our patent and patent applications covered our drug candidates that were internally discovered and developed by us. Up to the Latest Practicable Date, none of our patent applications had been rejected by the PRC and U.S. Patent Offices. We performed competitor landscape search for the inventions defined in our patent applications to determine whether our inventions are covered by any prior art and whether they are novel and potentially inventive, and the search results indicate high probability for obtaining patents for our Core Products. Our Industry Consultant, Frost & Sullivan, is also of the view that the competitor landscape search is commonly used and reliable means to estimate the probability of obtaining a patent in the pharmaceutical industry. In addition, we would like to highlight the inherent advantages associated with biological drugs, like our Core Products, in obtaining patent protection. Given the complexity and specificity of the structure and sequence of each biological drugs including our Core Products, it inherently possesses a distinctiveness that typically simplifies the patent approval process. Unlike small molecule drugs, which may face challenges due to the existence of numerous similar compounds, the unique sequence and structure of a biological drug makes it easily distinguishable, reducing the likelihood of overlaps with existing patents. Based on the inherent characteristics of our Core Products, we believe there is no foreseeable difficulties or legal impediments for us to obtain approvals for material patent applications, which is also in line with the general trends observed in the patenting of biologics. Even if our Group fails to obtain relevant patents, this would simply mean that the technology intended to be covered by such patent applications is not protected by patent rights, and we believe the loss of patent protection will not hinder us from developing and commercializing the drug candidates by using such technology, as well as our know-how and trade secrets in developing the drug candidates. Therefore, there is no material implication on our Group's business, financial position or results of operations. However, we cannot provide any assurance that patents will be issued with respect to any pending patent applications or any such patent applications that may be filed in the future. See also "Risk Factors — Risks Relating to Our Intellectual Property Rights" in this document for the impact on our business, financial position or results of operations if we eventually fail to obtain the relevant patents.

Our legal advisers as to intellectual property law, Jingtian & Gongcheng and Venture Partner, LLC, having checked and reviewed the legal status of the material patent applications, in the public online databases of the CNIPA, and World Intellectual Property Organization, and some other public patent databases as well as information provided by us regarding the pending patent applications, advised that they were not aware of foreseeable difficulties or legal impediments for us to obtain the relevant approvals for material patent applications, except that these patent applications remain subject to the examination opinions (if any) from the applicable patent examination authorities during the ordinary pendency and examination of such patent applications.

As further advised by legal advisers as to intellectual property law, given that obtaining relevant patents is not a prerequisite for our future R&D or commercial activities, the loss of patent protection (if any) will not hinder us from developing and commercializing the drug candidates by using the related technology, know-how and trade secrets in developing the drug candidate.

In addition, based on the results of the competitor landscape search, we have not identified any foreseeable risk of infringement by our Core Products against other major market player's patents or patent applications. During the Track Record Period and up to the Latest Practicable Date, we had not received any IP rights infringement complaints and our product candidates had not been subjected to any claim, litigation or investigation for any IP issue. Furthermore, our legal advisers as to intellectual property law have conducted the freedom-to-operate searches and analysis and did not identify any substantial risk of infringement by any current key technologies or features of our Core Products against any active patents in China and the U.S.

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

In addition, with respect to any issued patents in the U.S., China and certain other foreign jurisdictions, we may be entitled to obtain an extension of the patent's term provided we meet the applicable requirements for obtaining such patent term extensions. For example, in the U.S., we may apply for a patent term extension of up to five years as compensation for the patent term lost during clinical trials and the FDA regulatory review process under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The exact duration of the extension depends on the time we spend in clinical trials, as well as getting a BLA approval from the FDA. However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, a patent may be extended only once, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Furthermore, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. Furthermore, in China, the PRC Patent Law introduces patent extensions to patents of new drugs that launched in the PRC, which may enable the owner of the patent for an innovative new drug that has been granted the marketing authorization in China to submit applications for a patent term extension of up to a maximum length of five years, in order to compensate the time required for the regulatory approval for

the commercialization of such innovative new drug; provided that, the patent term of such innovative new drug shall not exceed a total of 14 years. In certain other foreign jurisdictions, similar extensions as compensation for regulatory delays are also available.

The actual protection afforded by a patent varies on a claim-by-claim and country-by-country basis and depends upon many factors, including the type of the patent, the scope of its coverage, the availability of any patent term extensions or adjustments, the availability of legal remedies in a particular country and the validity and enforceability of the patent. We cannot provide any assurance that patents will issue with respect to any of our 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 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.

We may rely, in some circumstances, on trade secrets and/or confidential information to protect our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with consultants, scientific advisors and contractors, and invention assignment agreements with our employees. We have entered into confidentiality agreements and non-competition agreements with our senior management and key members of our R&D team and other employees who have access to trade secrets or confidential information about our business.

These agreements may not provide sufficient protection of our trade secrets and/or confidential information. These agreements may also be breached, resulting in the misappropriation of our trade secrets and/or confidential information, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and/or confidential information may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to or successfully copy aspects of our products or to obtain or use information that we regard as proprietary without our consent. As a result, we may be unable to sufficiently protect our trade secrets and proprietary information.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. Despite any measures taken to protect our data and intellectual property, unauthorized parties may attempt to or successfully gain access to and use information that we regard as proprietary. For more details, see "Risk Factors — Risks Relating to Our Intellectual Property Rights" in this document.

We also own a number of registered trademarks and pending trademark applications. We have registered trademarks for our corporate logo in China and are seeking trademark protection for our corporate logo in the jurisdictions where available and appropriate.

During the Track Record Period and up to the Latest Practicable Date, (i) we were not involved in any legal, arbitral or administrative proceedings in respect of, and we had not received notice of any claims of infringement, misappropriation or other violations of third-party intellectual property; and (ii) we were not involved in any proceedings in respect of any intellectual property rights that may be threatened or pending and that may have an influence on the research and development for any of our drug candidates in which we may be a claimant or a respondent.

COMPETITION

The markets for biopharmaceutical industry, in particular, antibody products and fusion proteins, are evolving and highly competitive. While we believe that our research and development capabilities enable us to establish a favorable position in the industry, we encounter competition from international and domestic biopharmaceutical companies, specialty pharmaceutical and biotechnology companies of various sizes, academic institutions and research institutions.

We believe our principal competitive advantages are integration of proprietary R&D platforms, identification of promising targets, mechanisms and pathways for drug development, molecule screening and design, efficacy and safety of drug candidates, and manufacturing efficiency. We expect the competition will become more intensive in the future as additional players enter into these segments. Any drug candidates that we successfully develop and commercialize will compete with existing drugs or any new drugs that may become available in the future. For more information on the competitive landscape of our drug candidates, see "Industry Overview" in this document and "— Drug Candidates" in this section.

INSURANCE

We maintain insurance policies that we consider to be in line with market practice and adequate for our business. We maintain property insurance covering physical damage to, or loss of, our equipment; employer's liability insurance covering death or work injury of employees; and clinical trial insurance covering us against liability in the event of injury to any trial subject caused by serious adverse events in our clinical trial. For details, see "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" in this document.

We consider that the coverage from the insurance policies maintained by us is adequate for our present operations and is in line with the industry norm. During the Track Record Period, we had not made or been the subject of any material insurance claims.

EMPLOYEES

As of the Latest Practicable Date, we had 118 employees in total in China. The following table sets forth the number of our employees categorized by function as of the Latest Practicable Date.

Function	Number	Percentage of total
R&D	40	33.9%
CMC and Regulatory Affairs	57	48.3%
General and Administration	21	17.8%
Total	118	100.0%

We enter into individual employment contracts with our employees covering salaries, bonuses, employee benefits, workplace safety, confidentiality obligations, work product assignment clause and grounds for termination. We also enter into separate confidentiality and non-competition agreements 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.

To maintain our workforce's quality, knowledge, and skill levels, we also provide regular and specialized trainings tailored to the needs of our employees in different departments. We regularly organize training sessions conducted by senior employees or third-party consultants covering various aspects of our business operations including overall management, project execution and technical know-how. We also provide training programs to our employees from time to time to ensure their awareness and compliance with our policies and procedures in various aspects.

We are committed to making sure that working conditions throughout our business network are safe and that employees are treated with care and respect. Our employees' remuneration comprises salaries, bonuses, house provident funds, social insurance premium, and other welfare payments. Furthermore, we provide various incentives and benefits, including bonuses and share-based compensation, to our employees, particularly our key employees. We have made contributions to our employees' social insurance premium (including pension plans, medical insurance, work-related injury insurance, unemployment insurance and maternity insurance) and housing provident funds pursuant to applicable laws and regulations. Certain of our practices is not in full compliance with relevant statutory social insurance premium and housing provident fund obligations applicable to us under the PRC laws. See "Risk Factors — Risks Relating to Our Operations — Any failure to comply with the PRC regulations regarding contribution of social insurance premium or housing provident funds may subject us to fines and other legal or administrative measures" for more information. As of the Latest Practicable Date, we had not received any order of correction or any fines or

penalties from the competent authority as a result of any such failure. We have obtained certain confirmation letters issued by the relevant competent social insurance and housing provident fund authorities confirming that there is no record of any member of our Group that hires employees being imposed administrative penalties by the relevant authorities for violation of the relevant laws and regulations. As advised by our PRC Legal Adviser, the likelihood that we will be required to settle all historical social insurance premiums and housing provident funds and be subject to material administrative penalties due to our failure to make full contributions of social insurance premium and housing provident funds for some of our employees during the Track Record Period is relatively low, provided that there are no material adverse changes in the current regulatory policies and environment and no material employee complaints occur.

As of the Latest Practicable Date, our employees were represented by a labor union. We believe that we maintain a good working relationship with our employees. During the Track Record Period, we did not have any strikes, protests or other material labor conflicts that may materially affect our business and image.

LAND AND PROPERTIES

As of the Latest Practicable Date, we had entered into a state-owned construction land use rights grant contract with Planning and Natural Resources Bureau (規劃和自然資源局) in Nanjing for a parcel of land with a total site area of approximately 26,524.8 sq.m. We were in the process of obtaining the land use right certificate for such land. As of the Latest Practicable Date, we leased two properties with an aggregate GFA of approximately 8,070.6 sq.m., which were primarily used for offices, R&D and manufacturing. We believe our current facilities are sufficient to meet our near-term needs, and additional space can be obtained on commercially reasonable terms. We do not anticipate undue difficulty in renewing our leases upon their expiration.

The following table sets forth the details of our leased property as of the Latest Practicable Date:

Location	Type of Property	GFA	Lease Term
		(sq.m.)	
Nanjing	Office/R&D center/ Manufacturing Plant	8,000	April 1, 2023 – March 31, 2028
Huzhou	Office	70.6	October 15, 2023 – October 14, 2026

As of the Latest Practicable Date, our lease in Huzhou had not been filed with competent governmental authority. For details of risks relating to our leased properties, see the section headed "Risk Factors — Risks Relating to Our Operations — We do not own the real property for our current major operation sites and are subject to risks associated with leasing space" in this document.

We do not have any property interest with a carrying amount of 15% or more of our consolidated total assets as of December 31, 2023. Therefore, according to Chapter 5 of the Listing Rules and [**REDACTED**] of the Companies (Exemption of Companies and Prospectuses from Compliance with Provisions) Notice (Chapter 32L of the Laws of Hong Kong), this document is exempted from compliance with the requirements of section 342(1)(b) of the Companies (Winding Up and Miscellaneous Provisions) Ordinance in relation to paragraph 34(2) of the Third Schedule to the Companies (Winding Up and Miscellaneous Provisions) Ordinance which requires a valuation report with respect to all of our interests in land or buildings.

AWARDS AND RECOGNITIONS

We have received various awards and recognitions for our projects and entities. The following table sets forth the selected awards and projects as of the Latest Practicable Date:

Year of Grant	Project/Entity	Award/Recognition	Issuing Authority
2023	SunHo (China) BioPharmaceutical	Top 50 in China's Biologics R&D Strength Ranking in 2023	2023 Conference on the High-quality Development of the Health Industry
2021	IAH0968	Provincial Key Research and Development Plan (Social Development) Project (Project Announcement No. 168)	Jiangsu Provincial Department of Science and Technology
2021	IAP0971	Nanjing Life and Health Technology Special Project – Breakthrough in Clinical Frontier Technology	Nanjing Municipal Science and Technology Bureau

OCCUPATIONAL HEALTH, SAFETY AND ENVIRONMENTAL MATTERS

Overall

We are committed to operating our business in a manner that protects the environment and providing our employees with a healthy and safe workplace.

We will comply with the environmental, social and governance ("**ESG**") reporting requirements after [**REDACTED**] and the responsibility to publish ESG report on an annual basis in accordance with Appendix C2 to the Listing Rules. We will focus on each of the areas as specified in Appendix C2 to the Listing Rules to analyze and disclose important ESG matters, risk management and the accomplishment of performance objectives, particularly those environmental and social issues that could have a material impact on the sustainability of our operations and that are of interest to our Shareholders. Specifically, we have implemented the following measures with respect to hazardous waste discharge: (i) requiring

proper handling and disposal of hazardous waste; (ii) setting up hazardous waste storage sits in accordance with relevant standards and establish standardized hazardous waste management system; and (iii) engaging qualifies third-party suppliers for waste disposal. In addition, we will adopt the following measures to mitigate environmental impact from our business, strategy and financial performance in the near, medium and long term, as summarized below:

Area	Key Measures
Energy and resource conservation	• Introduces new environmental equipment and gradually phases out energy-intensive facilities • Update technologies for energy conservation and environmental protection • Improve energy recycling
Sewage and solid waste management	• Recycle the packaging materials • Improve sewage treatment mode
Greenhouse gas management	• Increase the use of clean energy • Use energy efficient equipment
Exhaust gas management	• Adopt exhaust gas treatment system and install active carbon filters

We have implemented company-wide environmental, health and safety ("**EHS**") manuals, policies and standard operating procedures. In particular, our EHS protection measures include (i) strict compliance with the GMP qualification requirements and relevant pollutant emissions standards and pollutants management policies during our production process to reduce pollutant emissions of exhaust gas, sewage and hazardous solid waste; (ii) implementation of safety guidelines with respect to employee health and safety, environmental protection and operational and manufacturing safety in laboratories and manufacturing facilities, and closely monitor internal compliance with these guidelines; (iii) storage of hazardous substances in special warehouse and contract with qualified third parties for the disposal of hazardous materials and waste; (iv) conducting periodic environmental evaluations on exhaust gas detection and emissions, hazardous waste disposals, noise emissions, and waste water detection and emissions to make sure all operations are in compliance with the applicable laws and regulations; and (v) resource conservation policies to reduce the levels of resource consumption.

As we are currently at an early stage of laboratory operations and partially rely on CROs for testings, clinical trials and other activities, the current nature of our business does not expose us to a substantial risk of environmental, health or work safety matters, and we do not expect the potential risks of such matters will have a material adverse impact on our business operation and financial performance.

Environmental Protection

The pollutants produced during our production process mainly include filtered fermentation broth, purified buffer solution, disposable cell culture bags, deep filter membrane bags and used solid waste. The filtered fermentation broth and purified buffer solution themselves do not contain any toxic substances and could be discharged safely into the sewage treatment plant for processing. Depending on mature sewage treatment technology, we have made sewage treatment a routine part of our production process. The solid waste is disposed of by qualified third-party waste recycling institutions. The local environmental protection department regularly inspects our production activities and waste emissions and no material administrative penalties imposed on us had been found that may have a material adverse effect on our business operations during the Track Record Period and up to the Latest Practicable Date.

We endeavor to reduce negative impact on the environment through our commitment to energy saving and sustainable development. We actively promote the idea of a paperless workplace, and we encourage double-sided printing of documents in our office. With our future business expansion, we focus on the balance between business growth and the need of ESG to achieve sustainable development. The relevant material metrics for our resource consumption will be reviewed regularly to ensure that they remain appropriate to the needs of our Group. While we appreciate that the identification and prioritization of ESG-related issues is a dynamic and on-going process, we will build the following targets as our initial focuses:

- To reduce the level of power and water consumption density;
- To advocate green office and make full use of natural lighting, and provide energy-efficient solutions for air conditioning;
- To strictly abide by the laboratory "three waste" treatment implementation standards;
- To provide ESG-related training for our staff members, with at least two working days per person per year.

In the upcoming future, our relevant expenses regarding environmental, social, and climate-related issues are estimated to increase, along with our overall business development, however, the proportion of such expenses against our total revenue is estimated to trend downwards.

During the Track Record Period and up to the Latest Practicable Date, we had not received any fines or penalties associated with the breach of any environmental laws or regulations. To the best knowledge and belief of our Directors, we are not subject to material environmental liability risk and will not incur material compliance costs in the future.

Resource Consumption and Pollutant Disposals

We monitor the following metrics to assess and manage the environmental and climate-related risks arising from our business and manufacturing operations:

- *Electricity consumption*. We have monitored our electricity consumption levels and implement measures. In 2022 and 2023, our electricity consumption levels were 1.0 million kWh and 1.4 million kWh, respectively.

- *Water consumption*. We have monitored our water consumption levels and implement measures to promote water conservation during the Track Record Period. In 2022 and 2023, our water consumption levels were 7.0 thousand tons, and 18.0 thousand tons, respectively.

- *Hazardous waste discharge*. We have a safety administrator who monitors and manage our hazardous waste storage and disposal. We have also contracted with qualified third-party waste disposal company for the disposal of hazardous material and waste. As of the Latest Practicable Date, a total of 0.1 tons of hazardous waste was stored in our warehouse and was overseen by our safety administrator. Considering our storage capacity and cost efficiency, we will transfer hazardous waste to the waste disposal company once we accumulated considerately large amount of waste.

In setting targets for the ESG-related KPIs, we will take into account our respective historical consumption or discharge levels during the Track Record Period, and our future business expansion in a thorough and prudent manner with a view of balancing business growth and environmental protection to achieve sustainable development. We will make continuous efforts in working towards the target of reducing our electricity and water consumption and hazardous wastes discharge per thousand dollars of R&D expense by 5% in 2024.

Greenhouse Gases Emissions

We aim to reduce our greenhouse gases ("**GHG**") emissions and contribute to the transition to a low-carbon economy. We adhere to the "3R" approach to environmental conservation, i.e. reduction of waste, reuse of resources and recycling of used materials, to the extent possible in our business operation. The GHG emissions of various scopes are respectively generated from the fuel consumption of vehicles of our Group (Scope 1), power consumption (Scope 2), water consumption, waste discharge, paper consumption and GHG

emission resulting from the business travel of our employees (Scope 3) during business operation. Our Group's GHG emission results principally from Scope 2 energy indirect GHG emission which is power consumption to support our operations, and Scope 3 other indirect emissions.

We will implement measures in mitigating the GHG emissions, including (i) providing trainings and educate our employees on the concept of energy efficiency; (ii) posting water-saving or power-saving signs in eye-catching areas to cultivate our employees' awareness of environment protection; (iii) promoting paperless environment, encourage the usage of electronic copies instead of hard copies, the use of double-sided printing, and the use of single-sided printed paper when there is no confidential information on it; (iv) requiring employee to turn off all electrical appliances when they are not in use; and (v) implementing policies regarding waste management.

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 (i) acute physical risks, such as increased severity of typhoon or floods; and (ii) 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.

We have made disaster preparedness plans for the extreme events and will closely monitor our business operation 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. Due to the nature of our business, we are not prone to material impacts of chronic physical risks or transition risks.

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.

Employee Health and Safety

We also emphasize providing a safe working environment for our employees and clinical trial participants. We incorporate work safety guidelines on safe practices, accident prevention and accident reporting as core aspects of our employee training and induction processes, and we ensure that clinical trial participants properly acknowledge their understanding of safety matters at the time of enrollment and on an ongoing basis as necessary. In addition, we have adopted and maintained a series of rules, standard operating procedures and measures to

maintain a healthy and safe environment for our employees, including those required under the GMP standards. Furthermore, we conduct safety inspections of our laboratories and manufacturing facilities on a regular basis. Last but not least, we established an occupational health and monitoring management system, for the protection of the health and rights of our employees, prevention of occupational diseases, and proper placement and compensation for employees diagnosed with occupational diseases.

During the Track Record Period and up to the Latest Practicable Date, we had not been and were not involved in any material non-compliance incidents regarding the environmental and occupational health and safety laws and regulations that have led to fines or penalties that could, individually or in the aggregate, have a material adverse effect on our business, financial condition, and results of operations, and we did not have any workplace accident.

Workforce Welfare and 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 the Latest Practicable Date, we had 118 employees, among whom more than 60% were female. In addition, more than 40% of our employees aged over 30 and more than 5% aged over 50. Our employees boast a diverse range of experiences and professional backgrounds, encompassing areas such as biomedicine, biochemistry, pharmaceutical engineering, food quality and engineering, immunology, genetics, financial management, human resources, intellectual property, and international trade, among others. We adhere to a fair and transparent employee management system and strive to enhance gender and age diversity of our workforce.

We established human resources management policies that systematically outline the recruitment processes, promotion procedures, dismissal/resignation processes, performance evaluation approaches, retention strategies, salary and benefits procedures, employee training, etc. In particular, we stick to our corporate governance philosophy of "valuing, attracting, nurturing, and employing talents appropriately." Our implement a merit-based hiring approach so make sure our recruitment is based on the principles of openness, fairness, and equity.

Supply Chain Management

Our suppliers primarily include raw material suppliers and contract services providers. Our considerations in supply chains include technical quality, cost effectiveness, delivery efficiency and reliability. Accordingly, we define risks related to supply chains consisting of shortage of raw materials, workforce health and safety incidents, proper disposal of hazardous waste, and internal control for corruption and bribery.

To identify and cope with any potential risks, we established procurement management policies that clearly define the overall review and regular evaluation processes for suppliers, based on which we made a qualified supplier list and update the list from time to time. Additionally, we established management policies in relation to procurement of technical contract services that specifies the responsibilities for the service providers, including CROs, testing organizations, clinical trial centers, etc. The policies also outline due diligence procedures, selection criteria, approval process, performance management and payment settlement. Furthermore, we tend to opt for scaled suppliers that are public companies as we believe such partners are subject to stricter compliance standards and capable of offering more environmentally-friendly products and services. We have also implemented strict anti-corruption and anti-bribery policies to prevent collusion and corruption.

Governance on EHS Matters

We have a dedicated group level EHS team under the supervision of our senior management responsible for overseeing our compliance with EHS related regulations and policies, and monitoring our implementation of related internal measures, such as: (i) adopting appropriate safety measures at our facilities and implementing best practice procedures; (ii) conducting regular safety awareness training to our employees; (iii) inspecting our facilities regularly to identify and eliminate any potential safety hazards; (iv) adopting appropriate procedures regarding the disposal of any hazardous waste such as Waste Management Procedure, which aims to effectively manage the waste generated during our normal course of business, standardize the classification of the waste into solid waste and hazardous waste according to the relevant laws and regulations and dispose them accordingly to reduce environmental pollution; (v) maintaining a system of recording and handling accidents in our facilities; and (vi) cooperating with regulatory authorities for the regular environmental compliance monitoring. Our EHS team may assess or engage independent third party(ies) to evaluate the ESG risks and review our existing strategies, targets and internal controls at least once a year. Necessary improvement will then be implemented to mitigate the risks.

Our EHS department to implement the national and our own safety production and environmental protection guidelines, and follow up with the instructions or notice from local authorities with regard to fire protection, safety supervision and environmental protection in a timely manner, as well as formulate our Company's safety production policies and operating procedures. The management personnel at all levels and all of our employees will implement the work responsibility system according to EHS related regulations and policies, and related internal measures.

Social Responsibility

In respect of social responsibilities, it is our corporate policy to offer equal opportunities to our employees regardless of gender, age, race, religion or any other social or personal characteristics. We strive to operate our facilities in a manner that protects the environment and the health and safety of our employees and communities.

PERMITS, LICENSES AND OTHER APPROVALS

Our PRC Legal Adviser has advised that, as of the Latest Practicable Date, we have obtained all licenses, permits, approvals and certificates from the relevant PRC government authorities that are material to our operations in the PRC. The table below sets forth the relevant details of the material license we hold for our operations in China.

License	License No.	Date of Expiration	Issuing Authority
Drug Manufacturing License (藥品生產許可證)	SU20180566 (蘇20180566)	December 20, 2025	Jiangsu Medical Products Administration

LEGAL PROCEEDINGS AND COMPLIANCE

We may from time to time be involved in contractual disputes or legal proceedings arising out of the ordinary course of business or pursuant to governmental or regulatory enforcement actions. During the Track Record Period and up to the Latest Practicable Date, neither we nor any of our Directors were involved in or subject to any litigation, arbitration, administrative proceedings, claims, damages or losses which would have a material adverse effect on our business, financial position or results of operations as a whole. As of the Latest Practicable Date, we were not aware of any pending or threatened material litigation, arbitration or administrative proceedings against us or any of our Directors, which individually or as a whole would have a material adverse effect on our business, financial position or results of operations.

During the Track Record Period and up to the Latest Practicable Date, we had complied, in all material respects, with relevant PRC laws and regulations in the jurisdictions we operate in, and no material administrative penalties were imposed on us.

RISK MANAGEMENT AND INTERNAL CONTROL

Risk Management

We are exposed to various risks in our business operation and we recognize that risk management is critical to our success. For details, see "Risk Factors — Risks Relating to Our Operations" in this document. Additionally, we are faced with credit risk, liquidity risk and market risks including currency risks credit and interest rate risk, all of which are inherent in the ordinary course of our business. See "Financial Information — Market Risk Disclosure" in this document for detailed discussion. We have adopted a series 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 ongoing 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 Company and reported to our Directors. Our audit committee, and ultimately our Directors supervise the implementation of our risk management policies.

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

- establish an Audit Committee to review and supervise our financial reporting process and internal control system;

- adopt various policies to ensure compliance with the Listing Rules, including but not limited to aspects related to risk management, connected transactions and information disclosure; and

- attend training sessions in respect of the relevant requirements of the Listing Rules and duties of directors of companies [**REDACTED**] in Hong Kong.

Intellectual Property Risk Management

We have designed and adopted strict internal procedures to ensure the compliance of our business operations with the relevant rules and regulations, as well as the protection of our intellectual property rights.

In accordance with these procedures, our legal counsel performs the basic function of reviewing and updating the form of contracts we enter into with our customers and suppliers. Our legal counsel as well as business operation teams examine the contract terms and reviews all relevant documents for our business operations, including licenses and permits obtained by the counterparties or us to perform contractual obligations and all the necessary underlying due diligence materials, before we enter into any contract or business arrangements.

Our regulatory affairs team reviews our products and services, including upgrades to existing products, for regulatory compliance before they are made available to the general public. Our regulatory affairs team is responsible for obtaining any requisite governmental pre-approvals or consent, including preparing and submitting all necessary documents for filing with relevant government authorities within the prescribed regulatory timelines and ensuring all necessary application, renewals or filings for trademark, copyright and patent registration have been timely made to the competent authorities.

Internal Control

Our Board is responsible for establishing our internal control system and reviewing its effectiveness. We have engaged an independent internal control consultant (the "**Internal Control Consultant**") to perform certain agreed-upon procedures (the "**Internal Control Review**") in connection with the internal control in certain aspects, including entity-level

controls, financial reporting and disclosure controls, human resources and payroll management, general controls of IT system and other procedures of our operations. The Internal Control Consultant performed the Internal Control Review and identified internal control deficiencies and provided recommendation accordingly. We have adopted the corresponding remediation actions to improve the effectiveness of internal control system. The Internal Control Consultant performed a follow-up review with regard to those actions taken by us and there are no further material findings identified in the process of the follow-up review. As of the Latest Practicable Date, there were no material outstanding issues relating to our Company's internal control.

During the Track Record Period, we reviewed and enhanced our internal control system on a regular basis. 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 risk management, protection of intellectual property, environmental protection and occupational health and safety. We provide periodic training about these measures and procedures to our employees as part of our employee training program. We 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 [**REDACTED**].

- We [have established] an audit committee which, among others, (i) makes recommendations to our Board of Directors on the appointment and removal of external auditors; and (ii) reviews the financial statements and internal control system of our Company.

- We have engaged Somerley Capital as our compliance adviser to provide advice to our Directors and management team until we distribute our annual report of financial results for the first full financial year after [**REDACTED**] regarding matters relating to the Listing Rules. We must consult with and if necessary, seek advice from our compliance adviser where we propose to use the [**REDACTED**] of the [**REDACTED**] in a manner different from our plan that sets forth in "Future Plans and Use of [**REDACTED**]" in this document after [**REDACTED**]. Our compliance adviser will also provide support and advice regarding requirements of relevant regulatory authorities in a timely fashion.

- We plan to provide various and continuing trainings to update our Directors, senior management, and relevant employees on the latest PRC laws and regulations from time to time with a view to proactively identify any concerns and issues relating to any potential non-compliance.

- We intend to maintain strict anti-corruption and anti-bribery policies and we believe we will therefore be less affected by the increasingly stringent measures taken by the PRC government to correct corruptive practices in the pharmaceutical industry.

We plan to provide our Directors, senior management, and relevant employees with continuous training programs and updates regarding the relevant applicable laws and regulations regularly and update our internal control policies in due course.

Data Privacy Protection

We have established procedures to protect the confidentiality of trial participants' data. We demand that all parties involved in clinical trials, both external and internal, adhere to confidentiality obligations. We require our personnel to collect and safeguard personal information in their possession. Our CROs and other partners are obligated to safeguard the confidentiality of such information pursuant to our contracts with them. Compliance with GCP and relevant rules ensures that only approved personnel can access clinical trial data. Data utilization is strictly confined to the use consented to by the patients, which is in line with the Informed Consent Form ("**ICF**"). We ensure to obtain further consent from patients for any data usage that extends beyond the ICF's scope.

Any data transfer related to our product development initiatives and regulatory communications must adhere to relevant local data protection and privacy laws. Accordingly, we have implemented a series of control measures and structures. These measures include ensuring the legality of the cross-border data transfers, securing necessary regulatory approvals, and making appropriate filings with competent authorities according to applicable laws and regulations (particularly in the case of any transfer between China and the U.S.). This is particularly important for data transfers between China and the U.S. Despite the evolving nature of these laws and our potential clinical trials, we have not encountered significant issues with data transfers so far. We believe our practices related to transferring clinical trial data between China and the U.S. conform to industry standards.

As confirmed by our PRC Legal Adviser, we were not subject to any material claims, lawsuits, penalties or administrative actions which had a material and adverse effect on our business, financial condition or results of operations in accordance with applicable PRC laws and regulations with respect to data privacy and protection.