## OVERVIEW

Founded in 2016, we are a science-driven, clinical-stage biotechnology company. We have established a comprehensive R&D infrastructure to accelerate the development of molecules from discovery to registrational trials. We have initiated one clinical trial and another five clinical trials for our Core Products LAE002 and LAE001. Among these six clinical trials, three multi-regional clinical trials (MRCTs) are designed to address medical needs in the standard of care (SOC)-resistant cancers.

### Our Market Opportunities

Although the field of cancer treatment has developed significantly in the past decade, a large proportion of cancer patients find themselves in the absence of effective or safe treatments. The quality of life of those patients is severely affected primarily attributable to SOC resistance and/or intolerable toxicity, resulting in a large unmet medical need and socioeconomic burden. Among those cancers of unmet medical needs, platinum-resistant ovarian cancer (PROC), metastatic castration-resistant prostate cancer (mCRPC), HR+/HER2- metastatic breast cancer (HR+/HER2- mBC) and triple negative breast cancer (TNBC) are some of the diseases with limited SOC options and undesirable treatment outcomes.

- PROC. According to Frost & Sullivan, the global and China incidence of ovarian cancer is expected to increase from 319.8 thousand and 56.2 thousand in 2021 to 374.2 thousand and 62.7 thousand in 2030, respectively. The SOC mainly consists of debulking surgery and platinum-based chemotherapy. Although platinum-based chemotherapy is normally effective at inducing an initial response, more than 80% of patients with epithelial ovarian cancer who achieve a full remission following first-line therapy will develop recurrent disease. PROC is broadly defined as ovarian cancer recurrence within six months of completing platinum-based chemotherapy, either in the primary or recurrent setting. PROC is generally associated with low response rates to standard chemotherapy with the overall response rate (ORR) of 10% to 15%, and median progression-free survival (PFS) of 3.5 months only, indicating limited effective treatment options and poor prognosis.

- mCRPC. According to Frost & Sullivan, the global and China incidence of prostate cancer is expected to increase from 1,451.5 thousand and 120.9 thousand in 2021 to 1,815.1 thousand and 199.3 thousand in 2030, respectively. Patients with prostate cancer that have relapsed after local therapy or that have distant metastasis usually respond to androgen deprivation therapy (ADT). However, despite receiving ADT, most of these patients eventually experience disease progression and develop castration-resistant prostate cancer (CRPC) within a median of 18 to 24 months from receiving ADT. A substantial majority of CRPC will develop into mCRPC. The current treatment regimen for mCRPC comprises of abiraterone acetate or enzalutamide, and abiraterone acetate requires co-medication with corticosteroids to manage adverse effects. Ultimately, almost all patients with mCRPC will develop drug resistance with limited treatment options.

- HR+/HER2- mBC and TNBC. According to Frost & Sullivan, the global and China incidence of breast cancer is expected to increase from 2,301.2 thousand and 336.3 thousand in 2021 to 2,666.4 thousand and 372.4 thousand in 2030, respectively. It is estimated that 60% of patients with breast cancer have HR+/HER2- molecular signature in China. The endocrine/anti-estrogen therapies in combination with CDK4/6 inhibitors have emerged as first- and second-line treatment for patients with HR+/HER2- breast cancer. However, 15% to 20% of patients are intrinsically resistant to treatment, and another 30% to 40% patients will develop acquired resistance to treatment over time, according to Frost & Sullivan. TNBC is a type of breast cancer that is estrogen receptor negative, progesterone receptor negative and human epidermal growth factor receptor 2 negative based on immunohistochemistry, which accounted for approximately 15% of the total breast cancer population globally. TNBC is primarily treated with systemic therapies (chemotherapies), immune checkpoint inhibitors (ICIs) and other targeted therapies. However, current treatments have relatively poor prognosis, high risk of recurrence, and no significant survival benefit, indicating huge unmet medical needs for the treatment of TNBC.

**Our R&D Approach**

To address these medical needs, we have developed our clinical and pre-clinical pipeline through a combination of internal discovery and asset in-licensing efforts. Based on our knowledge-based R&D approach, we have implemented a product development model that consists of internal discovery, business development and translational research.

- Internal discovery. Our internal drug discovery primarily focuses on identifying innovative immunology therapies for cancer and liver fibrosis. Our most advanced internally discovered cancer candidate is LAE102, a potentially potent and selective ActRIIA mAb that has demonstrated anti-tumor activity in pre-clinical animal models and increased body weight in cancer-bearing animals. Our most advanced internally discovered liver fibrosis candidate is LAE105, which is expected to target aHSC depletion and has advanced into proof-of-mechanism pre-clinical studies.

- Business development. We apply a disciplined approach for bolstering our existing pipeline and expanding our capabilities. We focus on clinically proven assets in cancer treatment where we have accumulated specialized knowledge and experience. As such, we obtained global rights from Novartis Pharma AG ("**Novartis**") on four clinical-stage drug candidates with a clinical proof-of-concept, namely LAE002, LAE001, LAE005 and LAE003. We will continue to expand our drug portfolio and explore partnership through strategic collaborations to maximize the value of our pipeline.

- Translational research. We devote substantial resources to conducting translational research on our in-licensed product candidates to expand their clinical applications. Our translational studies include indication expansions through combination therapies or providing targeted treatments through patient stratification. Specifically, we are conducting a Phase I/II trial for LAE001, prednisone and LAE002 combination therapy targeting drug-resistant mCRPC patients as second- to fourth-line treatments and a Phase I/II trial for LAE002 and LAE005 combination therapy for TNBC patients. We also redesigned LAE001's Phase I/II clinical trials to specifically target mCRPC patients without prior abiraterone acetate treatment.

We believe that this model will enable us to allocate our resources efficiently and effectively, and thus generate a pipeline of risk-mitigated products with clinical and commercial potential.

**Our Pipeline**

We have strategically developed a pipeline of 16 product candidates, including our Core Products LAE002 and LAE001. Our drug candidates are developed or aim to be developed as both monotherapy and combination therapy with a focus on the treatment of cancers and liver fibrosis. We have the exclusive global rights to develop, manufacture and commercialize LAE002, LAE001, LAE005 and LAE003 under our licensing agreement with Novartis. The following chart summarizes the development status of our clinical-stage drug candidates and selected pre-clinical-stage drug candidates as of the Latest Practicable Date.

Drug Candidate
Target Mechanism
Indications
Lead Discovery
Proof of Mechanism
CMC IND Enabling
Phase I
Phase II
Commercial Rights
Upcoming Major Milestones
Licensor/Partner
Cancer
Liver Fibrosis
Rare Disease
+ Paclitaxel
AKT + Chemotherapy
PROC (second- to sixth-line treatment)
MRCT (U.S. and China) | Registrational[1]
Global
NDA submission with the FDA and NMPA in 4Q 2023
NOVARTIS
+ LAE001 + Prednisone
AKT + CYP17A
mCRPC following SOC Treatment (second- to fourth-line treatment)
MRCT (U.S. and South Korea)[2]
Phase III initiation in 2H 2023
NOVARTIS
LAE002 + Sintilimab + Chemotherapy
AKT + PD-1 + Chemotherapy
PD-1/PD-L1 Resistant Solid Tumors
(3)
Phase I read-out in 4Q 2023
NOVARTIS innovent
+ LAE005 + Nab-Paclitaxel
AKT + PD-L1 + chemotherapy
TNBC (second- to third-line treatment)
(4)
Phase I read-out in 4Q 2023
NOVARTIS
+ Fulvestrant
AKT + ER
Locally Advanced or Metastatic HR+/HER2- Breast Cancer (second- to third-line treatment)
MRCT (U.S. and China)
(5)
NDA submission with the FDA and NMPA in 2H 2025
NOVARTIS
LAE001
CYP17A/CYP11B2
mHSPC (first-line treatment)
(6)
Phase II read-out in 3Q 2023
NOVARTIS
LAE102[8]
ActRIIA
Cancer
Phase I initiation in the U.S. in 1H 2024
LAE109
NK / T regulator
Cancer
IND application with FDA or NMPA by 4Q 2024
LAE111
NK / Ø regulator
Cancer
IND application with FDA or NMPA by 2Q 2024
LAE113
NK / T regulator
Cancer
IND application with FDA or NMPA by 2Q 2024
LAE117
NK / T regulator
Cancer
IND application with FDA or NMPA by 2025
LAE112
TAA
Cancer
IND application with FDA or NMPA by 3Q 2024
LAE118
Oncogenic signaling
Cancer
IND application with FDA or NMPA by 2025
LAE119
Synthetic lethality
Cancer
IND application with FDA or NMPA by 4Q 2024
LAE120
Synthetic lethality
Cancer
IND application with FDA or NMPA by 4Q 2024
LAE104
aHSC depletion
Liver Fibrosis
IND application with FDA or TGA by 2025
LAE105
aHSC depletion
Liver Fibrosis
IND application with FDA or TGA by 2025
LAE106
Conditional TGFß blocker
Liver Fibrosis
IND application with FDA or TGA by 2025
LAE003[7]
AKT
HHT/Proteus Syndrome
IND application with FDA and/or NMPA by 3Q 2023
NOVARTIS
Core Product
Internally Discovered
Global Rights Exclusively Licensed

*Notes:*

(1) The global MRCT Phase II trial would be the registrational trial and appropriate to support product registration. According to the written confirmation issued by FDA in February 2019 and by NMPA in February 2020, FDA and NMPA agreed that this global MRCT Phase II trial would be the registrational trial and appropriate to support drug registration if the clinical results demonstrate good efficacy and safety profile. We aim to make NDA submissions to the FDA and NMPA in the fourth quarter of 2023.

(2) The trial is a Phase I/II MRCT covering clinical sites in the U.S. and South Korea. Phase I study was completed in the U.S. in February 2021. We completed the patient recruitment in both the U.S. and South Korea in March 2023. Furthermore, the Phase III registrational trial for the same indication is planned to be a MRCT in the U.S., Asia and Europe, and we expect to initiate this MRCT in the U.S. first in the second half of 2023 and submit an NDA to the FDA and NMPA in 2025.

(3) This is a Phase I/II study with collaboration with Innovent in China, and currently in Phase I stage with patients enrolling. We plan to complete the Phase I study with preliminary results in the fourth quarter of 2023.

(4) This is a Phase I/II study in China, and currently in Phase I stage with patients enrolling. We plan to initiate the Phase II study in China in the first quarter of 2024 and complete the Phase II study in China in the fourth quarter of 2025. This study is planned to be expanded to a MRCT in China and the U.S. at the registrational stage.

(5) LAE002+fulvestrant Phase Ib/III study does not require a Phase II clinical trial prior to beginning registrational III clinical trials. This is a Phase Ib/III study in China and the U.S., and currently in Phase Ib stage in China and the U.S. with patients enrolling. We completed the recruitment of patients for the Phase Ib study in April 2023, and plan to initiate the MRCT Phase III study in China and the U.S. in the second half of 2023, with top-line results expected in the first half of 2025 and NDA submissions to the FDA and the NMPA in the second half of 2025.

(6) This is a Phase I/II study of LAE001 for mCRPC conducted only in China. We completed the Phase I study of LAE001 for mCRPC in China on September 13, 2021. We are currently conducting a Phase II clinical trial of LAE001 monotherapy on mCRPC. As part of our clinical development strategy for LAE001 in prostate cancer and based on the clinical data from trials on mCRPC, we plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S. and apply the NDA for mHSPC with the NMPA and the FDA in 2027.

(7) LAE003 has been conducted in several Phase I, Phase II clinical trials in various cancer indications prior to our in-licensing. We plan to repurpose the drug for rare disease indications with partners.

(8) We obtained the IND approval of LAE102 in May 2023.

*Glossary & abbreviations:*

PROC: platinum-resistant ovarian cancer; mCRPC: metastatic castration-resistant prostate cancer; mHSPC: metastatic hormone-sensitive prostate cancer; ER: estrogen receptor; TNBC: triple negative breast cancer; HHT: hereditary hemorrhagic telangiectasia

- Core Product LAE002. LAE002 is an ATP competitive AKT inhibitor. We in-licensed LAE002 from Novartis in 2018. Prior to our in-licensing, 11 clinical trials had been conducted to demonstrate the safety and efficacy profiles of LAE002 by Novartis and GSK plc. In the Phase I/II study conducted by Novartis, LAE002 showed potential anti-tumor efficacy in PROC patients. In pre-clinical studies, LAE002 has demonstrated its ability to restore platinum/paclitaxel sensitivity in PROC cell lines. After the in-licensing, we also identified the therapeutic potential of combining LAE002, prednisone and LAE001 and observed their synergistic anti-tumor efficacy in mCRPC patients as second- to fourth-line treatments. According to Frost & Sullivan, there are two AKT inhibitors that have entered registrational clinical trials globally.

- Core Product LAE001. LAE001 is an androgen synthesis inhibitor that inhibits both CYP17A1 and CYP11B2. We in-licensed LAE001 from Novartis in 2017. According to Frost & Sullivan, LAE001 is the only dual CYP17A1/CYP11B2 inhibitor in clinical trials for the treatment of prostate cancer globally. Our completed Phase I study showed safety, preliminary anti-tumor efficacy and potential clinical benefits for LAE001 monotherapy without the use of prednisone (long-term use or high dose exposure to prednisone may lead to adverse events) in mCRPC patients. We are currently conducting a Phase II clinical trial of LAE001 monotherapy on mCRPC. As part of our clinical development strategy for LAE001 in prostate cancer and based on the clinical data from trials on mCRPC, we plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S. and apply the NDA for mHSPC with the NMPA and the FDA in 2027.

- LAE005. LAE005 is expected to be a highly affinitive, ligand-blocking, humanized anti-PD-L1 IgG4 antibody. In pre-clinical and clinical studies, LAE005 demonstrated its binding avidity to PD-L1 and anti-tumor activities. Specifically, we are evaluating the therapeutic potential of the combination therapy of LAE002 and LAE005 in patients with TNBC. We believe LAE005 has the potential to serve as an effective therapy for the treatment of TNBC when combined with other synergistic mechanisms.

- LAE003. LAE003 is expected to be a potent ATP competitive AKT inhibitor. In the pre-clinical studies, LAE003 showed potency and selectivity to AKT1, AKT2 and AKT3. LAE003 is currently at the clinical stage for the treatment of cancer and we are re-purposing it for the treatment of hereditary hemorrhagic telangiectasia and proteus syndrome. We expect LAE003 to be our lead drug candidate in the rare disease therapeutic area.

- LAE102. LAE102 is our most advanced internally discovered drug candidate for cancer treatment. It is a potentially potent and selective activin receptor type IIA (ActRIIA) mAb that has demonstrated anti-tumor activity and ability to increase the bodyweight of cancer-bearing animals in pre-clinical animal models.

- LAE105. LAE105 is our most advanced internally discovered drug candidate for liver fibrosis treatment, which is expected to target activated hepatic stellate cells (aHSC) depletion and has entered into proof-of-mechanism pre-clinical studies.

**Our Team and Vision**

Our stable and seasoned core management team is instrumental to our continuous growth and development. Our core management team has established a long track record of accomplishment, leadership and deep knowledge in their respective fields. In addition, they share the common mission of discovering and delivering novel therapies to benefit patients worldwide. Our founder and Chief Executive Officer Dr. Chris Lu, Chief Medical Officer Dr. Yong Yue, and Chief Scientific Officer Dr. Justin Gu have known each other since college for 40 years and have worked extensively together, which lays solid foundation for our research and development as well as to create synergistic cooperation within our team.

With a vision to deliver novel therapies to patients worldwide, we have established an integrated team located in both China and the U.S. This arrangement allows us to be at the forefront of medical research and knowledge, conduct MRCTs efficiently and execute business development strategies. We are building in-house GMP-compliant manufacturing facilities in eastern China and aim to construct a supply chain system by leveraging our CMO partners in the U.S. and other regions. We have also established a clinical development and medical affairs function that allows us to rapidly execute our clinical trials and navigate the global regulatory environment to shorten the time to market for our product candidates. Since our inception, we have obtained over eight IND approvals from the FDA and NMPA and have initiated six clinical trials, including three MRCTs across China, the U.S. and other jurisdictions.

**STRENGTHS**

We believe the following strengths differentiate us from our competitors.

**ATP Competitive AKT Inhibitor LAE002 in Registrational Clinical Trials with Potentially Better Clinical Efficacy and Favorable Safety Profile**

LAE002, one of our Core Products, is an ATP-competitive AKT inhibitor. We have the exclusive global rights to develop, manufacture and commercialize LAE002 under our licensing agreement with Novartis. The upregulation of AKT pathway activity has been associated with SOC resistance in a number of cancers. AKT inhibitors have demonstrated their ability to reverse drug resistance in numerous clinical studies and showed their potential to address the urgent unmet medical needs in those selected cancers. Leveraging our in-depth knowledge and expertise of the AKT pathway activation, we have independently initiated five combination therapy clinical programs to evaluate the therapeutic potential of LAE002 in a variety of drug-resistant cancers, including PROC, mCRPC, breast cancer and PD-1/PD-L1 resistant solid tumors. According to Frost & Sullivan, the global and China market size of AKT inhibitors is expected to reach US$12,154.0 million and RMB14,674.4 million in 2030, respectively.

Prior to our in-licensing of LAE002, 11 clinical trials have already been conducted to evaluate the efficacy and safety of LAE002. Specifically, in the Phase I/II study of LAE002 in combination with carboplatin and paclitaxel for the treatment of PROC sponsored by Novartis, the overall response rate (ORR) was 32.1% and the median progression-free survival (PFS) was 7.1 months. We are conducting a registrational Phase II MRCT of LAE002 in combination with chemotherapy for PROC in the U.S. and China, and the preliminary data showed a favorable efficacy profile. As of the data cut-off date of February 13, 2022, a total of 44 subjects were evaluated for treatment response, including 30 subjects in arm 1 (LAE002 plus paclitaxel) and 14 subjects in arm 2 (paclitaxel). The ORRs in arm 1 and arm 2 are 33% and 14%, respectively.

Furthermore, according to Frost & Sullivan, LAE002 is one of the only two AKT inhibitors that have currently ongoing registrational clinical trials globally. Compared with capivasertib, the only other AKT inhibitor that currently has ongoing registrational clinical trials, LAE002 showed in non-head-to-head comparison of early phase clinical study results that it may have a better potency, bioavailability exposure and safety profile.

In our clinical trials, we also explored and discovered the therapeutic potential of the combination of LAE002 and LAE001 and observed their synergistic anti-tumor efficacy for the treatment of drug-resistant mCRPC. The second-generation androgen receptor antagonist enzalutamide has been approved for the treatment of mCRPC due to its significant improvement in overall survival. Unfortunately, not all patients with mCRPC are responsive to enzalutamide, and even in responders, benefits are limited by the development of drug resistance within one to two years' treatment. We are evaluating LAE002 in combination with LAE001 and chemotherapy for drug-resistant mCRPC patients. In the completed Phase I study, as of the data cut-off date of February 24, 2022, the median and maximum treatment periods without tumor progression of evaluable patients in RP2D cohort are 8.6 and 15.6 months, respectively. Among the 14 evaluable patients, two patients had a prostate-specific antigen (PSA) response. Among the five patients with measurable lesions, one achieved PR and two achieved SDs. This result suggests that the combination of LAE002 plus LAE001 and prednisone has a favorable efficacy profile in patients with drug-resistant mCRPC compared to the results of previous studies, where mCRPC patients who failed first- to third-line SOC had only two to four months of progression-free survival.

We believe LAE002 has the potential to become an effective therapy for drug-resistant breast cancer in the future and benefit a large population of patients. AKT activations such as PTEN loss and PI3KCA mutations have been reported to correlate with in approximately 60% of breast cancers, according to Frost & Sullivan. Phase II clinical studies conducted by multi-national companies, including Roche and AstraZeneca, have demonstrated favorable efficacy of their combination therapy of AKT inhibitors (i.e., ipatasertib and capivasertib) in the treatment of HR+/HER2- mBC and TNBC, respectively. We have observed preliminary anti-cancer activities in the Phase I combination trial of LAE002 plus LAE005 in TNBC patients. Another ongoing Phase Ib combination trial of LAE002 plus fulvestrant in HR+/HER2-mBC is expected to achieve comparable efficacy and safety clinical results, given LAE002's similar mechanism of action and safety profiles compared with ipatasertib and capivasertib.

## CYP17A1/CYP11B2 Inhibitor LAE001 Exhibits Favorable Efficacy Profile for Prostate Cancer

LAE001, our other Core Product, is a dual CYP17A1/CYP11B2 inhibitor. According to Frost & Sullivan, LAE001 is currently the only CYP17A1/CYP11B2 dual inhibitor candidate in clinical trials for prostate cancer treatment globally. We have the exclusive global rights to develop, manufacture and commercialize LAE001 under our licensing agreement with Novartis. We have completed our Phase I study and we are conducting a Phase II clinical trial to evaluate the efficacy and safety of LAE001 for mCRPC in China. We plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S., and submit NDA for LAE001 for the indication of mHSPC to the FDA and NMPA in 2027.

The current SOC for mHSPC and mCRPC consists mainly of chemotherapies and anti-androgen therapies including abiraterone acetate and enzalutamide. However, both abiraterone acetate and enzalutamide have long-term side effects and almost all mHSPC and mCRPC patients eventually develop acquired resistance, leaving them without effective treatment options. Abiraterone acetate, a CYP17A1 enzyme inhibitor, is currently approved only for use in combination with prednisone. However, a prolonged administration or high dose even for a short-term exposure of prednisone can cause severe adverse effects.

Given abiraterone acetate as a CYP17A1 enzyme inhibitor is not able to address CYP11B2 enzyme, it requires co-medication with corticosteroids to manage mineralocorticoid excess related adverse effects. In comparison, LAE001 has exhibited its high potency and selectivity against both the CYP17A1 and CYP11B2 enzymes in the pre-clinical studies. The CYP11B2 inhibitory activity of LAE001 could potentially reduce mineralocorticoids, which demonstrates its potential as a monotherapy without the co-administration with prednisone.

In a completed Phase I clinical trial sponsored by us, in the 50 mg BID (RP2D) Cohort, among 20 evaluable patients, 16 patients (80%) achieved over 50% reduction in PSA response and 12 patients (60%) achieved over 90% reduction in PSA response. In addition, LAE001 monotherapy demonstrated favorable safety profile in avoiding hyperaldosteronism associated symptoms.

The table below sets forth the clinical results of abiraterone combination therapy, LAE001 monotherapy for mCRPC. Although these were not head-to-head analyses, we believe that valuable insight can nonetheless be drawn from the comparison of our LAE001 with the abiraterone therapies.

| Trial ID and phase | NCT00473512 Phase II | NCT00474383 Phase II | NCT00485303 Phase II | NCT03843918 Phase I |
|---|---|---|---|---|
| **Study treatment** | Abi+Dexamethasone | Abi+Prednisone/ Prednisolone | Abi+Prednisone/ Prednisolone | LAE001 |
| **Patients (n)** | 42 | 47 | 58 | 20 |
| **Prior treatment** | | | | |
| Abi/Enza naïve | Yes | Yes | Yes | Yes |
| Docetaxel naïve | Yes | No (all 47 patients failed docetaxel) | No (all 58 patients failed docetaxel) | No (4/20 patients failed docetaxel) |
| **Median time to PSA progression (months)** | 7.4 | 5.6 | 5.6 | 12.9 |
| **PSA response** | | | | |
| >50% from baseline | 67% | 51% | 36% | 80% |
| >90% from baseline | 19% | 15% | 16% | 60% |

*Note:* No head-to-head comparison clinical study was conducted between drugs. Clinical trials of a drug cannot be directly compared to the clinical trials of another drug and may not be representative of the overall data.

*Glossary & abbreviation:*

Abi: abiraterone; Enza: enzalutamide

*Source: Company data G Attard, et al. 2009; AHM Reid, et al. 2010; AC Danila et al. 2010*

**Deep Understanding into Fundamental Disease Biology and Clinical Practice Empowers Our Internal Discovery, Business Development and Translational Research**

Backed by strong science-driven discovery, we aim to develop highly differentiated therapies. We prudently select and evaluate potential drug targets with strong biological and disease associations. We have implemented a product development model that leverages our in-depth understanding of disease pathogenesis, our business development network and our translational research capabilities. This strategy revolves around our science-driven R&D approach and is fueled by our unique scientific insight and in-depth knowledge into clinical practice and unmet needs.

- Internal discovery. We have a deep knowledge of disease biology, extensive experience in cutting-edge biological research, and an in-depth understanding of the clinical practice and medical needs. These enable us to identify therapeutic areas in hard-to-treat diseases and build a product pipeline with a risk-mitigated profile to address clinical pain points. We have assembled a seasoned and cross-national R&D team to support our continuous multi-source pipeline expansion. Our early discovery research is spearheaded by our Chief Scientific Officer, Dr. Justin Gu, an industry veteran with over 20 years of experience at multinational pharmaceutical companies, who has discovered multiple drug candidates during his tenure at the China Novartis Institute for Biomedical Research. Our internal drug discovery primarily focuses on identifying immunology therapies for cancer and liver fibrosis. LAE102 is our most advanced internally discovered drug candidate for cancer treatment, a potentially potent and selective ActRIIA mAb that has demonstrated anti-tumor activity in pre-clinical animal models and body weight gain in cancer-bearing animals. LAE105 is our most advanced internally discovered drug candidate for liver fibrosis treatment, which is expected to target aHSC depletion and has advanced into proof-of-mechanism pre-clinical studies.

- Business development. Over the past five years, we had a proven track record of building a global network and value-creating strategic partnerships and collaborations. We have established a number of global and regional partnerships with leading pharmaceutical companies, including Novartis and Innovent. Our partnerships cover various business collaboration models, including in-licensing and clinical collaboration. Our business development and R&D teams work closely to identify attractive business opportunities to optimize our pipeline structure in accordance with our product development strategy and R&D approach. Leveraging our understanding and scientific insights into cancer biology, we have successfully

in-licensed four clinically validated assets with strong combinatorial potential from Novartis, spearheaded by LAE002 and LAE001. In 2021, we entered into a collaboration agreement with Innovent to explore and maximize the potential value of the combination of LAE002 and sintilimab for patients with solid tumors in China. We believe such collaborations with leading pharmaceutical companies are a testament to our strong R&D capabilities.

- Translational research. We devote substantial resources to conduct translational researches on our licensed product candidates to expand their clinical applications. Our translational studies include expanding indications through combination therapies or providing more precise treatments through patient stratification. We are independently exploring multiple combination therapies for LAE002 that have not been previously validated to expand into. These efforts include studies of LAE002 in combination with LAE001 and prednisone for drug-resistant mCRPC patients as second- to fourth-line treatments, and LAE002 in combination with LAE005 for TNBC. In addition, following the in-licensing of LAE001, we have conducted extensive pre-clinical studies in collaboration with leading principal investigators (PIs) and key opinion leaders (KOLs) as well as research institutions to explore the monotherapy potential of LAE001. After obtaining favorable pre-clinical data, we redesigned the Phase I clinical trial of LAE001 specifically for patients with mCRPC who have not received abiraterone acetate therapy.

Leveraging our product development model, we have quickly built a broad and diversified pipeline of internally discovered and in-licensed drug candidates focused on cancer and liver fibrosis with potential to address significant unmet medical needs.

**Integrated Operations that Well-position us to Capture International Business Opportunities**

We have established an integrated R&D function in both China and the U.S. We have been able to stay at the forefront of biology and pharmaceutical research, source attractive business development opportunities, execute and closely manage complex MRCTs. Specifically, we have six clinical studies focusing on drug-resistant cancers, three of which are MRCTs. For the other three, we are conducting early phase clinical studies in China and we plan to expand the registrational trial once early phase clinical studies demonstrate proof of concept results.

As of the Latest Practicable Date, we had 82 employees in China and 10 employees in the U.S. Our clinical development and business development team in the U.S. are responsible for supervising and coordinating with CROs to support our clinical studies in the U.S., including these for LAE002, as well as seeking potential partners for collaboration. Our team in the U.S. also independently executes its day-to-day operations with respect to drug asset acquisition, corporate services and general functions. We have devoted significant resources, such as management time and attention, as well as financial and human resources, and taken certain integration measures in order to integrate operations in the U.S. and China. For example, we established an executive working group comprised of senior management personnel in China and the U.S. to foster close communications on ourstrategic plans and day-to-day

operations.With an aim to ensure that the U.S. team can share our resources and information, we have held a number of events to enhance the communication between our employees in the U.S. and China, and we have dispatched talents to the U.S. to support its operations. The interactions between our U.S. and China operations are a dynamic and mutually beneficial process with a goal to maximize our Group's performance as a whole.

Our management team provides us a strong presence in the network of pharmaceutical industry. Our management team has over six decades of combined experience working with multinational pharmaceutical companies, contributing to our successful in-license of four drug candidates from Novartis and our clinical collaboration with Innovent. Armed with our business development expertise and network, we can seek out-licensing opportunities to optimize our product pipeline and increase our return on invested capital. With presence in the key pharmaceutical markets and leveraging the expertise we have accumulated through our operations over the years, we are well positioned to capture strong industry growth opportunities in China and worldwide. Our clinical development and regulatory teams have extensive knowledge and experience in designing and executing clinical trials at all stages in indications with significantly unmet medical needs. In addition, our regulatory experience enables us to file IND applications and communicate with drug regulators more efficiently.

Leveraging on our integrated operation and collaborations with industry-leading CROs, SMOs and CDMOs, our teams of experts strive to accelerate drug development and bring promising therapies to China and worldwide. We entrust our seasoned clinical development team and lead local clinical trial partners to implement and execute our clinical development plan swiftly and conduct MRCTs. Since our inception, we have initiated six clinical trials and completed two clinical trials around the globe. In addition, we collaborate with PIs, KOLs, and physicians in clinical studies and basic research. With the support from frontline investigators, we strive to identify and validate new biomarkers, stratify patient populations, and expand addressable indications for our drug candidates. We also gain first-hand knowledge of clinical practice through our communication with leading medical scientists around the world, enabling us to identify unmet needs in overlooked disease areas. We have built strong business partnerships with leading CROs, CMOs and CDMOs in the U.S. and other regions. Furthermore, we are building in-house manufacturing facilities in eastern China to support the anticipated launches of our drug candidates.

**Seasoned Management Team with a Proven Track Record of R&D, Supported by Strategic Investors and Healthcare Specialists**

We have assembled a seasoned management team with extensive experience and expertise covering the full cycle of the clinical development process, from pre-clinical study design and clinical trial execution to regulatory processes and manufacturing. Our core management team has established a long track record of accomplishment, leadership and deep knowledge in their respective fields. In addition, they share the common mission of discovering and delivering novel therapies to benefit patients worldwide.

Our founder, Chairman and Chief Executive Officer, Dr. Chris Lu, is a seasoned pharmaceutical researcher with over 20 years of industry experience. He has a strong track record of developing successful drug candidates of both biologics and small molecules. With deep scientific knowledge and know-how in disease biology, translational research and drug development, he has co-invented more than 10 drug candidates, including bimagrumab, an antibody drug that earned "Breakthrough Therapy" designation from the FDA. In addition, Dr. Lu has extensive experience in the initiation and management of external collaboration with hospitals, academic institutes and CROs. He served as the executive director leading discovery biology platform and liver disease drug discovery at China Novartis Institute for BioMedical Research, and as the principal scientist and group head at Wyeth Research. Dr. Lu authored or co-authored more than 20 publications in peer reviewed journals.

Our Chief Medical Officer, Dr. Yong Yue has over 20 years of experience in oncology clinical development and ample clinical practice experience in China, Europe and the United States. Dr. Yue received his Doctor of Medical Science degree from the University of Geneva in Switzerland. Dr. Yue authored and co-authored more than 20 peer-reviewed publications.

Our Chief Scientific Officer, Dr. Justin Gu, has over 20 years of drug discovery experience in biotechnology and pharmaceutical companies with strong scientific background in cancer and liver disease. Before joining us, he served as a director of lead discovery at China Novartis Institute for BioMedical Research. Dr. Justin Gu is an experienced drug-hunter and key co-inventor of several pre-clinical drug candidates, some of which have successfully advanced into clinical studies. Dr. Justin Gu holds a Doctor of Philosophy degree in biochemistry from the Ohio State University and was a post-doctorate fellow at Massachusetts Institute of Technology before entering into the pharmaceutical industry.

We are also supported by our strong scientific advisory board consisting of leading scientists, physicians and industry veterans who have played key roles in shaping our R&D strategies and our involvement with the medical and industry communities. We are further supported by strategic and healthcare specialist investors such as Novartis and OrbiMed. They have provided us with invaluable guidance on product development, insights on strategic opportunities and the latest biomedical researches and clinical practices.

## STRATEGIES

We are committed to becoming a biopharmaceutical company that can bring novel therapies to cancer and liver fibrosis patients worldwide. To achieve our vision, we plan to pursue the following significant opportunities and execute our key strategies accordingly:

### Rapidly Advancing the Development of Our Existing Drug Candidates and Portfolio towards Commercialization

Leveraging our strong in-house clinical and development capabilities, we plan to continue to rapidly advance our existing clinical and pre-clinical drug candidates to achieve commercialization. To ensure smooth execution of our R&D process and to pursue a highly

efficient timetable towards commercialization, we have been and will continue to leverage on the massive patient pool in China and abroad. We will also continue to execute an innovative, tailored clinical trial design for each of our drug candidates by leveraging existing clinical data obtained through our in-license arrangements with other multinational pharmaceutical companies and strengthening our relationships with key external parties, including PIs, KOLs, CROs, SMOs, CDMOs, hospitals and others. We expect that our leading research in PROC, mCRPC and liver fibrosis treatments will continue to witness major milestones for our existing drug candidates in the near future.

We expect to continue to achieve and deliver major development milestones for our Core Products and key drug candidates, including LAE002, LAE001, LAE005 and LAE003 to further explore their potential. Particularly, we have formulated the following plans regarding our clinical-stage drug candidates.

- LAE002. We have initiated a global MRCT Phase II registrational trial in both the U.S. and China to treat PROC with LAE002, in a combination therapy with paclitaxel. As of the Latest Practicable Date, we had enrolled 144 subjects in both the U.S. and China. We aim to make NDA submissions to the FDA and NMPA in the fourth quarter of 2023.

  We initiated the Phase II trial of the Phase I/II MRCT study of LAE001 and prednisone plus LAE002 or docetaxel/prednisone plus LAE002 in patients with mCRPC following SOC treatment in the U.S. in June 2021. We initiated the same study in South Korea in September 2022. We completed the patient recruitment in both the U.S. and South Korea in March 2023. Furthermore, the Phase III registrational trial for the same indication is planned to be a MRCT in the U.S., Asia and Europe, and we expect to initiate this MRCT in the U.S. first in the second half of 2023 and submit an NDA to the FDA and NMPA in 2025.

  In addition, we are also actively exploring to further expand the indication of LAE002. We are with Innovent in exploring a combination therapy with sintilimab targeting patients with solid tumors with prior PD-1/PD-L1 treatments. We received the IND approval for this Phase I/II study from the NMPA in January 2022, and we initiated the Phase I study in June 2022. We plan to complete the Phase I study and the analysis of the preliminary results in the fourth quarter of 2023. We are also conducting a Phase Ib/III trial in China and the U.S. for the treatment of locally advanced or metastatic HR+/HER2- breast cancer with LAE002, in a combination therapy with fulvestrant. We completed the recruitment of patients for the Phase Ib study in April 2023, and plan to initiate the MRCT Phase III study including China and the U.S. in the second half of 2023, with top-line results expected to become available in the first half of 2025 and NDA submissions to the FDA and the NMPA in the second half of 2025.

- LAE001. We are currently conducting a Phase II clinical trial of LAE001 monotherapy on mCRPC. As part of our clinical development strategy for LAE001 in prostate cancer and based on the clinical data from trials on mCRPC, we plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S. and apply the NDA for mHSPC with the NMPA and the FDA in 2027.

- LAE005. We have initiated a Phase I/II trial in China for the treatment of TNBC in combination with LAE002 and nab-paclitaxel to continue to leverage the clinical value and explore AKT's potential. We plan to obtain the Phase I read-out in the fourth quarter of 2023, initiate the Phase II study in China in the first quarter of 2024 and complete the Phase II study in China in the fourth quarter of 2025. This study is planned to be expanded to a MRCT trial in China and the U.S. at the registrational stage.

- LAE003. We are re-purposing LAE003 for rare diseases such as hereditary hemorrhagic telangiectasia and Proteus syndrome. To further discover the therapeutic potential of LAE003, we are exploring potential opportunities to cooperate with global partners on the development of LAE003.

**Actively Exploring Potential Combination Therapy Opportunities to Fully Unlock Clinical Value of Our Product Pipeline**

To recognize the distinct values of our clinical drugs and fully capture their clinical potential, we will continue to actively explore potential combination therapy opportunities among our pipeline and with existing approved drugs as well as conventional therapies.

Our experience in executing and developing combination therapies among our pipeline, such as LAE002 and LAE001, to treat the second-generation A/AR drug-resistant mCRPC has well demonstrated our ability to unleash the clinical value of our pipeline products. Studies have shown that prostate cancer progression is associated with an increased frequency of PTEN deletion, suggesting that in addition to the androgen/androgen receptor signaling pathway, PTEN deletion leads to castration resistance in prostate cancer during androgen deprivation therapy. LAE002, a strong AKT inhibitor, overcomes the PTEN deficiency-mediated increase in AKT activity. We hypothesized that combining LAE002 with LAE001 and androgen synthesis inhibitors may have therapeutic effects for patients with PTEN-deficient mCRPC. To validate our hypothesis, we designed and conducted a series of combination trials of LAE002 and LAE001, the latest of which being the Phase II MRCT currently being conducted in the U.S. and South Korea. We expect to expand our drugs' indications, improve efficacy via synergies, and potential lower toxicity. Besides, to complement our product portfolio and realize synergies via a combination strategy, we expect to continue our in-licensing activities and seek long-term collaborations to bring in high-value, disruptive and differentiated products with clinical values and attractive risk-return profiles.

In addition, we plan to continue to explore combination opportunities with marketed drugs, as represented by PD-1/PD-L1 and conventional treatments. Acknowledging the resistance and limited efficacy of PD-1/PD-L1 therapies to a large group of patients, we have been and will continue to discover combination therapies by leveraging our differentiated small molecules with clear proof of concept. We are currently conducting clinical studies of LAE002 in combination with sintilimab or LAE005 to treat TNBC and solid tumors after anti-PD-1/PD-L1 therapy, respectively. To further our current studies of LAE002 in combination with paclitaxel and docetaxel, we will also keep exploring the possibility of combination therapies with endocrine therapy to treat hormone-related cancers without any or optimal solutions. Furthermore, we also intend to initiate clinical developments in HR+/HER2- breast cancer.

**Consistently Expanding Our Drug Pipeline through In-House Discovery to Address Broader Underserved Patients**

The global drug clinical development landscape has become increasingly competitive. Based on our deep industry knowledge, seasoned experience in the R&D process, and the know-how accumulated from our successful clinical development, we will continue to seek innovative solutions in the field of cancer and liver fibrosis with significant unmet medical needs. To leverage our knowledge in these disease areas and build synergies between programs targeting both disease indications, we are focusing our research on immune cells that are important for immune surveillance in cancer and fibrosis reversal in liver fibrosis. We are developing multiple monoclonal and bispecific antibodies against key regulatory pathways of NK cells and T cells and bifunctional NK engagers against cancer cells and activated hepatic stellate cells. They are in various stages of drug discovery, and we plan to have at least one molecule to enter the clinical stage each year on average, starting in 2023.

- Cancer drug candidates. Although ICIs have been approved for first- and second-line treatment for a variety of cancer indications worldwide, most patients with solid tumors do not respond to or eventually develop resistance to ICI therapy. We are developing immuno-oncology agents that target the mechanisms that mediate resistance to first-generation ICIs. Among these, we are particularly interested in the inhibitory receptors expressed by cancer infiltrating lymphocytes (i.e., LAE102, LAE109, LAE111, LAE113 and LAE117) and ligands/receptors expressed on or produced by cancer cells (i.e., LAE112). We believe that these inhibitory pathways represent targets for developing anti-tumor agents that could reverse resistance to ICIs.

  Our most advanced candidate is LAE102, an activin receptor ActRIIA mAb. As a member of the TGFβ family, activin is attracting an increasing interest due to its multifunctional role in cancer development, particularly its immunomodulatory function. In several cancer types, high expression of activin is associated with shorter survival. LAE102 is a potentially potent and selective ActRIIA mAb that has demonstrated anti-tumor activity and its ability to increase the bodyweight of cancer-bearing animals in pre-clinical animal models.

- Liver fibrosis drug candidates. In addition to our pre-clinical-stage cancer drug candidates, we are also developing a number of pre-clinical drug candidates for liver fibrosis which represent another huge unmet medical need. Recent evidence suggests that liver fibrosis can be reversed by regulating the immune system. We have established a proprietary aHSC depletion platform to remove aHSC for fibrosis regression. Bi-functional aHSC-NK engagers or regulators (i.e., LAE104 and LAE105) with aHSC killing and anti-fibrosis activity have been developed. We have also designed and validated a TGFβ inhibitor, LAE106, active only in fibrotic tissues. All of these molecules have the potential to slow or prevent the progression of liver fibrosis, and their utility may be expanded to other fibrotic diseases.

**Further Enhancing Our Capabilities as Our Clinical Studies Progress and Business Develops**

With our existing operations in both China and the U.S., we plan to further enhance our capabilities by building our platform with comprehensive coverage of the full cycle of the clinical development process, complemented by synergistic business development activities. We have adopted and intend to accomplish the following multi-layered plans to support our global strategy.

- R&D. We are dedicated to leveraging our expertise to further enhance our drug discovery and clinical development capabilities. Currently, we have two R&D centers in China and the U.S. We will continue to expand both facilities to take advantage of talents, technology and information acquired in both regions to feed and sustain the continued growth of our pipeline. Besides, we plan to actively engage with PIs, KOLs, CROs, SMOs, CDMOs and hospitals to carry out and expand global multi-center trials for our existing candidates and ultimately to pursue a global registration strategy.

- Manufacturing. We plan to establish strong manufacturing capabilities to support the near-term launch of our product candidates. To achieve this goal, we plan to build a cGMP-compliant manufacturing site in eastern China, focusing on manufacturing small molecule products. We will also collaborate with leading CMOs and CDMOs to complement our in-house CMC capabilities. Besides, we also plan to diversify our supply chain for equipment and raw materials to reduce cost and increase manufacturing efficiency.

- Sales and Marketing. We target to build sales and marketing capabilities through a combination of an in-house strategy and partnering with leading industry participants, especially our existing licensing and collaboration partners. With respect to our in-house efforts, we intend to build a sales and marketing team of about 50 members to provide dedicated coverage of Class III Grade A hospitals in top-tier cities in China. Upon successful launch of our products and continuous penetration in these targeted hospitals, we will further expand our reach intolower-tier cities to maximize the commercial value of our drug candidates. With respect to

external partnerships, we will explore out-licensing opportunities especially in lower-tier cities in China or other key global markets. Further, we will keep actively seeking and maintaining collaborations with other top global and local healthcare companies, academic institutions, and scientific research centers to promote our marketing activities in different targeted regions, including the Europe, Japan, and other regions.

- Business Development. We will keep seeking strategic collaborations that bring value to our pipeline. We plan to continue to seek assets through in-licensing arrangements, both in clinical and preclinical stage that complement our pipeline. A strong emphasis will continue to be placed on assets that could offer us global development and commercialization rights, have potential combination synergies with our current pipeline, and/or have first-in-class potential. As our late-stage assets are close to commercialization, we will also seek assets with commercial synergies with our late-stage pipeline. We will also consider pursuing business collaborations with other global partners in terms of joint development and commercialization of our drug candidates in international markets.

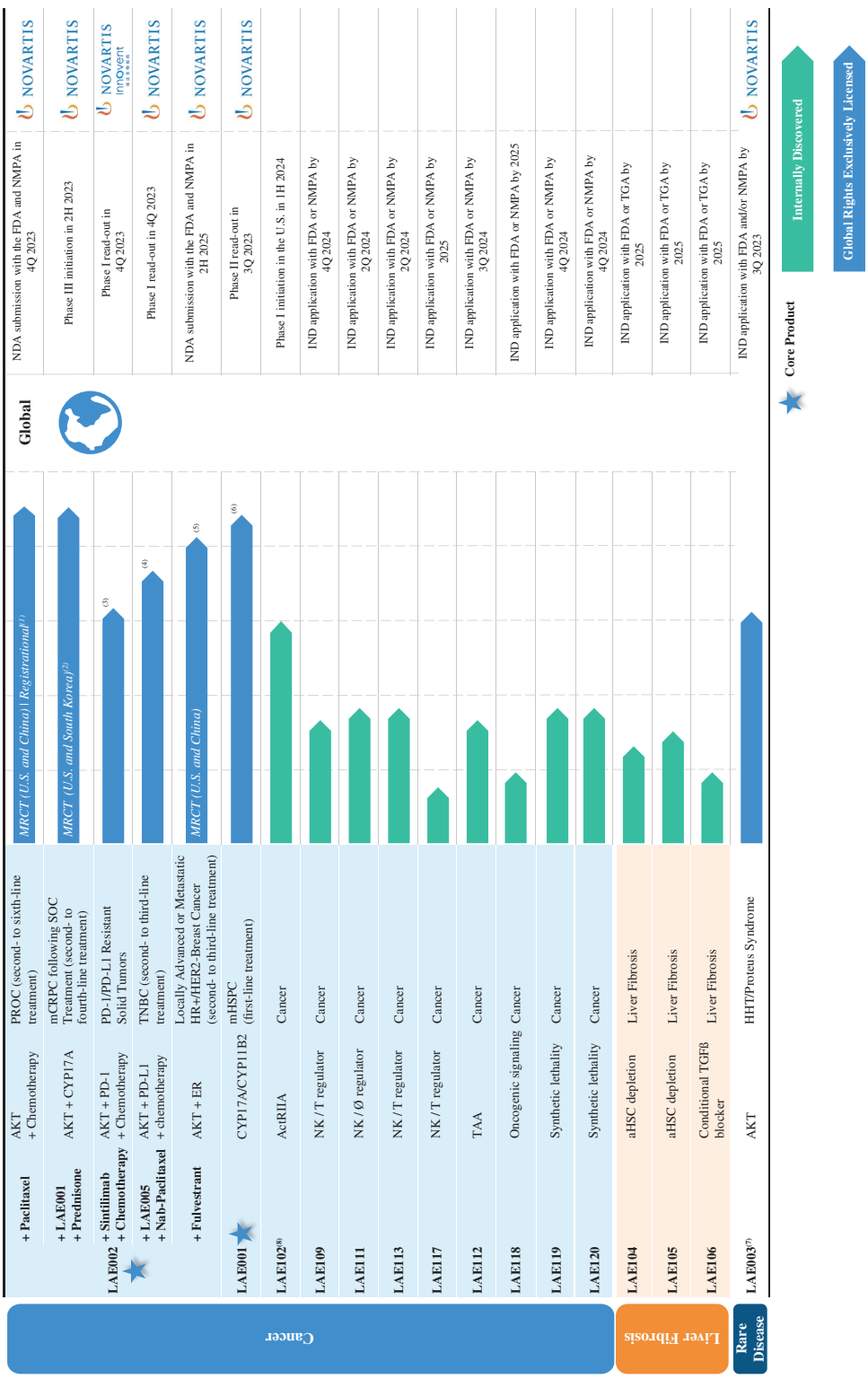
**Continuing to Attract and Retain Top Talents and Become a World-Class Global Organization**

We place a strong emphasis on talent recruitment and retention. We recognize that talents are key to our future success and sustainable growth. To support our aspiration to becoming a world-class organization, we will continue to recruit and train top talents especially those with experience from large multinational pharmaceutical companies and with expertise in clinical development, R&D, CMC and commercialization of our drug candidates. To achieve that end, we will continue to foster our culture of innovation, collaboration and efficiency and refine our organizational structure to empower our leaders and team members to take ownership of their respective work and reward their contributions. We will also strive to provide the training to nurture our young members to become future key opinions in the pharmaceutical industry. Our highly skilled talents in both China and the U.S. will work closely to transform us into a world-class organization.

## DRUG CANDIDATES

As of the Latest Practicable Date, we have strategically designed and developed a diversified pipeline of 16 programs with R&D and commercialization rights. Our pipeline includes four in-licensed clinical-stage assets and 12 pre-clinical stage assets.

The following chart summarizes the development status of our clinical-stage drug candidates and selected pre-clinical-stage drug candidates as of the Latest Practicable Date:



*Notes:*

(1) The global MRCT Phase II trial would be the registrational trial and appropriate to support product registration. According to the written confirmation issued by FDA in February 2019 and by NMPA in February 2020, FDA and NMPA agreed that this global MRCT Phase II trial would be the registrational trial and appropriate to support drug registration if the clinical results demonstrate good efficacy and safety profile. We aim to make NDA submissions to the FDA and NMPA in the fourth quarter of 2023.

(2) The trial is a Phase I/II MRCT covering clinical sites in the U.S. and South Korea. Phase I study was completed in the U.S. in February 2021. We completed the patient recruitment in both the U.S. and South Korea in March 2023. Furthermore, the Phase III registrational trial for the same indication is planned to be a MRCT in the U.S., Asia and Europe, and we expect to initiate this MRCT in the U.S. first in the second half of 2023 and submit an NDA to the FDA and NMPA in 2025.

(3) This is a Phase I/II study with collaboration with Innovent in China, and currently in Phase I stage with patients enrolling. We plan to complete the Phase I study with preliminary results in the fourth quarter of 2023.

(4) This is a Phase I/II study in China, and currently in Phase I stage with patients enrolling. We plan to initiate the Phase II study in China in the first quarter of 2024 and complete the Phase II study in China in the fourth quarter of 2025. This study is planned to be expanded to a MRCT in China and the U.S. at the registrational stage.

(5) LAE002+fulvestrant Phase Ib/III study does not require a Phase II clinical trial prior to beginning registrational III clinical trials. This is a Phase Ib/III study in China and the U.S., and currently in Phase Ib stage in China and the U.S. with patients enrolling. We completed the recruitment of patients for the Phase Ib study in April 2023, and plan to initiate the MRCT Phase III study in China and the U.S. in the second half of 2023, with top-line results expected in the first half of 2025 and NDA submissions to the FDA and the NMPA in the second half of 2025.

(6) This is a Phase I/II study of LAE001 for mCRPC conducted only in China. We completed the Phase I study of LAE001 for mCRPC in China on September 13, 2021. We are currently conducting a Phase II clinical trial of LAE001 monotherapy on mCRPC. As part of our clinical development strategy for LAE001 in prostate cancer and based on the clinical data from trials on mCRPC, we plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S. and apply the NDA for mHSPC with the NMPA and the FDA in 2027.

(7) LAE003 has been conducted in several Phase I, Phase II clinical trials in various cancer indications prior to our in-licensing. We plan to repurpose the drug for rare disease indications with partners.

(8) We obtained the IND approval of LAE102 in May 2023.

*Glossary & abbreviations:*

PROC: platinum-resistant ovarian cancer; mCRPC: metastatic castration-resistant prostate cancer; mHSPC: metastatic hormone-sensitive prostate cancer; ER: estrogen receptor; TNBC: triple negative breast cancer; HHT: hereditary hemorrhagic telangiectasia

## CLINICAL STAGE CANDIDATES

### Core Product LAE002: An ATP Competitive AKT Inhibitor

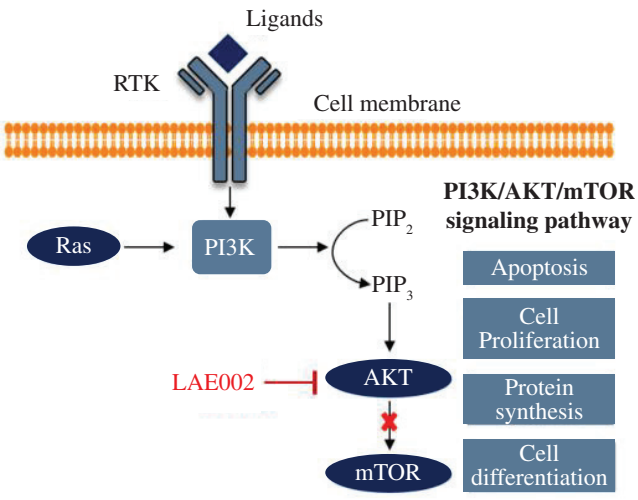
#### *Overview*

LAE002 is an ATP competitive AKT inhibitor. We in-licensed LAE002 from Novartis in 2018. Prior to our in-licensing, 11 clinical trials had been conducted to demonstrate the safety and efficacy profiles of LAE002 by Novartis and GSK plc. In particular, in a Phase I/II study conducted by Novartis, LAE002 showed potential anti-tumor efficacy in PROC patients. In pre-clinical studies, LAE002 has demonstrated its ability to restore platinum/paclitaxel sensitivity in PROC cell lines. After the in-licensing, we also identified the therapeutic potential of combining LAE002, prednisone and LAE001 and observed their synergistic anti-tumor efficacy in mCRPC patients as second- to fourth-line treatments. According to Frost & Sullivan, there are two AKT inhibitors that have entered registrational clinical trials globally.

#### *Mechanism of Action*

AKT is a serine/threonine-protein kinase with three isoforms (AKT1, AKT2 and AKT3) that participate in multiple pathways regulating several cellular processes, including survival, proliferation, tissue invasion, and metabolism. Aberrant activation of the AKT pathway occurs in almost every type of human malignancy, suggesting that deregulation of these pathways may be required for carcinogenesis. The importance of AKT-mediated pathways in tumor proliferation and survival renders AKT kinases promising targets for therapeutic intervention. Somatic activation of the PI3K/AKT signaling pathway most commonly occurs through activating mutations in PIK3CA (which encodes the catalytic p110α kinase subunit) or through loss-of-function mutations, deletions or promoter methylation silencing of the tumor suppressor gene PTEN (a negative regulator of PI3K). Less frequently, mutations in AKT (e.g., AKT1 E17K) can be a transforming and potentially targetable event across various solid tumors. Non-clinical data suggest that blocking AKT activity can inhibit the proliferation of tumor cells, and may either induce an apoptotic response or sensitize tumors to undergo apoptosis in response to other cytotoxic agents. LAE002 is an oral, low nanomolar pan-AKT kinase inhibitor that has been shown to inhibit the proliferation of a range of tumor cell lines from multiple histologies, including breast, hematological, colon, ovarian, and prostate. Resistance to cytotoxic chemotherapy may be mediated by various mechanisms, including induction of AKT activity, which leads to a pro-survival/anti-apoptotic state.

The diagram below sets forth the mechanism of action of LAE002.




*Notes:* RTK receptor protein tyrosine kinase; mTOR: mammalian target of rapamycin; $PIP_2$: phosphatidylinositol(4,5) bisphosphate; $PIP_3$: phosphatidylinositol-3,4,5-triphosphate

*Source: Frost & Sullivan analysis*

### *Market Opportunity and Competition*

*Market Opportunities of LAE002 in Combination with Chemotherapy for PROC*

According to Frost & Sullivan, the global and China incidence of ovarian cancer is expected to increase from 319.8 thousand and 56.2 thousand in 2021 to 374.2 thousand and 62.7 thousand in 2030 respectively. The current SOC mainly consists of debulking surgery and platinum-based chemotherapy with or without bevacizumab or PARP inhibitor. Although platinum-based chemotherapy is effective at inducing an initial response, more than 80% of initially responding tumor will recur, and resistance to platinum-based therapy will eventually emerge. PROC is broadly defined as primary ovarian cancer recurrence within six months of completing platinum-based chemotherapy, either in the primary or recurrent setting.

Many patients continue to respond to second-line platinum-based chemotherapy, and following the response, the guideline-recommended approach for many patients is surveillance, monitoring patients for disease progression and managing their symptoms. After relapse, it is observed that patients respond moderately or poorly to subsequent chemotherapy, with later lines of therapy leading to progressively shorter treatment-free intervals.

We are currently evaluating LAE002 in combination with chemotherapy for PROC, which has shown favorable efficacy and safety profiles. We believe LAE002 in combination with chemotherapy has the potential to be the SOC in second-line treatment for PROC.

*Market Opportunities of LAE002 in Combination with LAE001 + prednisone or Chemotherapy for mCRPC*

According to Frost & Sullivan, the global and China incidence of prostate cancer is expected to increase from 1,414.3 thousand and 114.3 thousand in 2020 to 1,815.1 thousand and 199.3 thousand in 2030, respectively. Most of the prostate cancer patients receiving androgen deprivation therapy eventually experience disease progression and develop CRPC within a median of 18 to 24 months from receiving the therapy, and a substantial majority of CRPC will be developed into mCRPC.

The current treatments for mCRPC can be broadly classified into four categories based on their mechanisms of action: (i) anti-microtubule drugs such as docetaxel. Docetaxel acts mainly through the suppression of microtubule dynamic assembly and disassembly. Docetaxel has shown relatively more serious side effects as a chemotherapy drug, including allergic reactions, myelosuppression, digestive tract reactions, fluid retention and angioedema, cardiovascular toxicity, fatigue and tearing; (ii) radiation therapies such as xofigo (Radium 223 dichloride), an alpha particle-emitting pharmaceutical, which is a radiotherapeutic drug that the FDA only approved for the treatment of mCRPC with bone metastases. It may not be suitable for treating mCRPC patients with visceral metastases; (iii) CYP17A1 enzyme irreversible inhibitors such as abiraterone; and (iv) AR inhibitors such as enzalutamide.

The second-generation anti-androgen agent enzalutamide has been approved for the treatment of mCRPC, in both post- and pre-docetaxel settings, due to the significant improvement in overall survival rate. More recently, enzalutamide also showed impressive results in the treatment of men with non-mCRPC. Unfortunately, not all patients with mCRPC are responsive to enzalutamide, and even in responders, benefits are limited by the development of drug resistance, which may be caused by PTEN/PIK3CA/AKT alterations. We are evaluating the combination therapy of LAE002 with LAE001 and prednisone or LAE002 with chemotherapy for drug-resistant mCRPC patients, which is intended to benefit patients with PTEN/PIK3CA/AKT alterations.

*Market Opportunities of LAE002 in Combination with Immune Checkpoint Inhibitors (ICIs) for Multiple Solid Tumors*

In the cancer-immunity cycle, the immune checkpoint proteins act as accomplices to help tumors resist immunity-induced apoptosis and promote tumor progression. Although ICIs have been approved for the treatment of a variety of cancer indications worldwide, only a limited proportion of patients would respond to immunotherapies. For instance, the objective response rate to PD-1/PD-L1 therapy was 30-45% in melanoma, 15-20% in NSCLC, 13% in head and neck carcinoma, and 22-25% in kidney cancer. This necessitates an improved immunotherapy regimen that could further exploit the immune system for cancer treatment. As a serine/threonine kinase, AKT is viewed as a potential new target for cancer treatment. The results of multiple pre-clinical studies have shown that inhibiting AKT can restore the sensitivity of cancer cells to oncology therapies.

Among these solid tumors, TNBC is a type of breast cancer that is tested estrogen receptor (ER) negative, progesterone receptor (PR) negative and human epidermal growth factor receptor 2 (HER2) negative based on immunohistochemistry (IHC). It is characterized by a shorter overall survival rate and an early peak in distant recurrences three years after diagnosis. According to Frost & Sullivan, the global incidence of TNBC increased from 306.7 thousand in 2017 to 345.2 thousand in 2021 at a CAGR of 3.0%, and the incidence of TNBC in China increased from 47.3 thousand in 2017 to 50.4 thousand in 2021 at a CAGR of 1.6%. Currently, TNBC is primarily treated with systemic therapy (chemotherapy), ICIs and antibody-drug conjugates. In the early study, the ORR of the ICIs treated PD-L1 expression group (CPS>=10) is 52.7% only, indicating there is still a large proportion of patients who do not respond to ICIs (initial resistance). Although pembrolizumab treatment has improved median PFS in PD-L1 expression group for patients with metastatic TNBC (9.7 months in the pembrolizumab treatment group vs. 5.6 months in the placebo group), the initial responders eventually develop resistance to ICIs therapy (secondary resistance). Therefore, both primary- and secondary-resistant to ICI treatment account for the majority of TNBC patients. Our combination therapy of LAE002 and LAE005 is expected to improve the clinical efficacy of ICIs by reducing the AKT activity in cancer cells and also selectively activated T-cells, which can suppress tumor growth and reduce metastasis.

We are currently evaluating the efficacy and safety of the combination of LAE002 and sintilimab or ICIs in patients with specific types of PD-1/PD-L1 drug-resistant solid tumors. We believe our combination therapy will provide a new treatment option for patients with solid tumors who are resistant to treatment with PD-1/PD-L1 inhibitors.

*Market Opportunities of LAE002 in Combination with Estrogen Receptor Antagonists for HR+/HER2- Breast Cancer*

According to Frost & Sullivan, it is estimated that 60% of patients with breast cancer have HR+/HER2- molecular signature in China. The treatment and management of HR+/HER2- breast cancer largely depend on early diagnosis and timely medical intervention. The endocrine/anti-estrogen therapies in combination with CDK4/6 inhibitors have emerged as first- and second-line treatment for patients with HR+/HER2- breast cancer. However, 15–20% of tumors are intrinsically resistant to treatment, and another 30–40% acquire resistance to treatment over time. Combination therapies based on LAE002 and estrogen receptor antagonists are being explored in clinical trials in patients with various types of drug-resistant HR+/HER2- breast cancer. We believe that the new treatment options will be well-positioned to capture the large therapeutic potential and opportunity and address unmet medical demands of HR+/HER2- breast cancer.

*Competitive Landscape*

According to Frost & Sullivan, no AKT inhibitor candidates are currently approved for commercialization globally. A summary of the global competitive landscape of AKT inhibitors under clinical development for cancer, as well as their indications of interest, is set forth below:

**Pipeline Globally**

| INN/Drug Code | Company | Phase* | First Post Date** | Indication*** |
|---|---|---|---|---|
| Capivasertib | AstraZeneca | III | 2019/6/25 | Prostate Cancer (III, HSPC), locally advanced or metastatic breast cancer (III), triple negative breast neoplasms (III), Non-Hodgkin Lymphoma (II), endometrial cancer (II), meningioma (II) |
| **LAE002 (Afuresertib)** | **Laekna** | **II (Registrational)** | **2020/5/5** | **PROC (II), mCRPC(II), Locally advanced or metastatic HR+/HER2-breast cancer (Ib/III), PD-1/PD-L1 inhibitor resistant solid tumor (I/II)** |
| Ipatasertib | Roche | II | 2020/07/13 | NSCLC (II), gastric cancer (II), ovarian cancer (II, R/R epithelial OC), glioblastoma multiforme (I/II), endometrial cancer (I/II) |
| TAS-117 | Taiho Oncology | II | 2021/2/25 | Advanced or metastatic solid tumors (excluding primary brain tumors) harboring germline PTEN inactivating mutations |
| M2698 | EMD Serono | I | 2013/10/29 | Solid tumors |
| TAS0612 | Taiho Oncology | I | 2020/10/14 | Advanced or metastatic solid tumors |
| WGI-0301 | HaichangBiotech | I | 2022/3/07 | Advanced Solid Tumors |

*Notes:*

* Phase refers to the drug's most advanced phase stage of all ongoing studies.

** First posted date denotes the date when the most advanced clinical stage of a clinical trial for an indication is first publicly announced. Information as of April 30, 2023.

*** The chart shows cancer indications only.

*Source: ClinicalTrials.gov, Frost & Sullivan analysis*

The following table presents the status of AKT inhibitor candidates at clinical-stage in China:

**Pipeline in China**

| INN/Drug Code | Company | Phase* | First Post Date** | Indication*** |
|---|---|---|---|---|
| Capivasertib | AstraZeneca | III | 2020/10/9 | Metastatic HSPC (III), Metastatic CRPC (III), TNBC (III), HR+/HER2-Locally Advanced or Metastatic Breast Cancer (III) |
| **LAE002 (Afuresertib)** | **Laekna** | **II (Registrational)** | **2020/11/19** | **PROC (including fallopian tube carcinoma and primary peritoneal carcinoma) (II), TNBC (I/II), HR+/HER2-Locally Advanced or Metastatic Breast Cancer (Ib/III), PD-1/P1-L1 resistant solid tumor (I/II)** |
| NTQ1062 | Chia Tai Tianqing | I | 2021-08-18 | Advanced solid tumor |

*Notes:*

* Phase refers to the drug's most advanced phase stage of all ongoing studies.

** First posted date denotes the date when the most advanced clinical stage of a clinical trial for an indication is first publicly announced. Information as of April 30, 2023.

*** The chart shows cancer indications only.

*Source: CDE, Frost & Sullivan analysis*

The following sets forth the global and China competitive landscape of our Core Product LAE002:

## AKT Targeting Drug Clinical Data for Prostate Cancer

| Company | Drug | NCT number | Phase | Indication | No. of patients | Treatment Line | Intervention/ Treatment | Median Follow-up Duration (month) | Median Overall Survival (month) | Median Progression-Free Survival (month) | Objective Response Rate | Adverse Event Rate (≥G3) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Roche | Ipatasertib | NCT01485861 | I/II | CRPC | 253 | 2L | Ipatasertib + Abiraterone | NA | 400mg – 18.92<br>200mg – 21.5 | 400mg ipatasertib – 8.18<br>200mg ipatasertib – 8.31 | 400mg – 32.4%<br>200mg – 23.1% | 400mg – 64.3%<br>200mg – 50.6% |
| AstraZeneca | Capivasertib | NCT04493853 (Ongoing) | III | HSPC | 1000 | 1L | Capivasertib + Abiraterone | NA | NA | NA | NA | NA |
| | | NCT02121639 (ProCAID) | II | mCRPC | 150 | ≥1L | Capivasertib + Docetaxel | 23.7 | 31.2 | 7.0 | NA | 62.2% |
| | | NCT02525068 | I | mCRPC | 15 | ≥2L | Capivasertib + Enzalutamide | NA | NA | NA | 20% | NA |
| | | NCT04087174 | I | mCRPC | 15 | ≥2L | Capivasertib + Abiterone | NA | NA | NA | 20% | NA |
| Laekna | LAE002 (Afuresertib) | NCT04060394* | I/II | mCRPC | 15 | ≥2L | LAE001 or docetaxel/ prednisone + afuresertib | 12.5 | NA | NA | NA | 67% |

*Note:*

* The results are from the completed Phase I study, and Phase II study is ongoing.

Only trials with results published by April 30, 2023 were included. Trial data were obtained from the literature and public information, not head-to-head trials, and comparisons are for informational purposes only. AstraZeneca is currently conducting a Phase III clinical trial of capivasertib for mHSPC.

## AKT Targeting Drug Clinical Data for PROC

| Company | Drug | NCT number | Phase | Indication | No. of patients enrolled | Treatment Line | Intervention/ Treatment | Median Follow-up Duration (month) | Median Overall Survival (month) | Median Progression-Free Survival (month) | Overall Response Rate | Adverse Event Rate (≥G3) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Laekna | LAE002 (Afuresertib) | NCT01653912 | I/II | PROC | 59 | ≥2L | Afuresertib + Carboplatin + Paclitaxel | NA | NA | 7.1 | 32.1% (RECIST)<br>52% (CA-125) | 76% |
| | | NCT04374630 (Ongoing) | II | PROC | 61 | ≥2L | Afuresertib + Paclitaxel | NA | NA | NA | 33% | NA |

*Note:* Information as of April 30, 2023. Only trials with results published by April 30, 2023 were included. Trial data were obtained from the literature and public information, not head-to-head trials, and comparisons are for informational purposes only.

The NCT01653912 Phase I/II trial was conducted by Novartis using the three-drug combination of LAE002, carboplatin and paclitaxel based on preliminary favorable efficacy of the component drugs. Carboplatin is usually responsible for more severe safety events as compared to paclitaxel when used in a combination therapy. Therefore, for PROC, given that the two-drug combination of "LAE002 and paclitaxel" may

potentially have a better safety implication and similar efficacy for patients, we selected the two-drug combination in our Phase II global registrational trial for PROC (NCT04374630). During the communication with regulatory authorities on the Phase II global registrational trial design, they also had no objection to the selection of the two-drug combination therapy. The preliminary efficacy result of 33% overall response rate with the two-drug combination therapy from our Phase II clinical trial indeed reported a similar efficacy as compared to 32.1% overall response rate with the three-drug combination therapy from the Novartis Phase I/II trial.

## AKT Targeting Drug Clinical Data for TNBC

| Company | Drug | NCT number | Phase | Indication | No. of Patients | Treatment Line | Intervention/ Treatment | Median Follow-up Duration (month) | Median Overall Survival (month) | Median Progression-Free Survival (month) | Objective Response Rate | Adverse Event Rate (≥G3) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Roche | Ipatasertib | NCT02162719 (LOTUS) | II | TNBC | 166 | 1L | Ipatasertib + Paclitaxel | 19.0 | 25.8m | 6.2m | 40% | 28% (SAE) |
| AstraZeneca | Capivasertib | NCT02423603 (PAKT) | II | TNBC/mBC | 140 | 1L/2L | Capivasertib + Paclitaxel | 18.2 | 19.1 | 5.5 (intention-to-treat subgroup) 7.6 (PIK3CA/ AKT1/ PTEN - Altered subgroup) | 34.8% (intend-to-treat subgroup) 35.3% (PIK3CA/ AKT1/ PTEN- Altered subgroup) | 54% |
| | | NCT03742102 (BEGONIA) | I/II | mTNBC | 220 (E) | 1L | Capivasertib + durvalumab + paclitaxel (Arm2) | NA | NA | NA | 53.5% | 73% |
| | | NCT03997123 (CAPItello-290) | III | TNBC | 800 (E) | ≥1L | Capivasertib + Paclitaxel | NA | NA | NA | NA | NA |
| Laekna | LAE002 (Afuresertib) | NCT05390710 | I/II | mTNBC | 101(E) | ≥1L | LAE005 + LAE002 + Nab-Paclitaxel | NA | NA | NA | NA | NA |

*Note:* Information as of April 30, 2023. Only trials with results published by April 30, 2023 were included. Trial data were obtained from the literature and public information, not head-to-head trials, and comparisons are for informational purposes only. The clinical trial results of the Phase III trial of capivasertib and the Phase I trial of LAE002 (afuresertib) for TNBC are not publicly disclosed yet.

## AKT Targeting Drug Clinical Data for HR+/HER2-BC

| Company | Drug | NCT number | Phase | No. of patients | Indication | Treatment Line | Intervention/ Treatment | Median Follow-up Duration (month) | Median Overall Survival (month) | Median Progression-Free Survival (month) | Objective Response Rate | Adverse Event Rate (≥G3) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Roche | Ipatasertib | NCT03959891 | Ib | 60 | HR+/HER2 - mBC | ≥2L | Fulvestrant + Ipatasertib + Palbociclib | NA | NA | NA | 17% | NA |
| AstraZeneca | Capivasertib | NCT04305496 (CAPItello-291) | III | 834 | HR+/HER2- mBC | ≥1L | Capivasertib + Fulve strant | NA | NA | 7.2 | 22.9% (28.8% in AKT pathway-altered population) | Diarrhea-9.3%, maculopapular rash-6.2%, rash-5.4%, hyperglycemia 2.3%, stomatitis 2.0% |
| | | NCT01992952 | II | 140 | ER+mBC after AI | ≥2L | Capivasertib + Fulve strant | 4.9 | 23.7m | 10.3m | 29% | NA |
| Laekna | LAE002 (Afuresertib) | NCT04851613 | Ib | 20(E) | HR+/HER2- mBC | ≥2L | LAE002 + Fulvestrant | NA | NA | NA | NA | NA |

*Note:* Information as of April 30, 2023. Only trials with results published by April 30, 2023 were included. Trial data were obtained from the literature and public information, not head-to-head trials, and comparisons are for informational purposes only. The Phase III trial of capivasertib for HR+/HER2- is ongoing and the clinical trial results of the Phase Ib trial of LAE002 (afuresertib) for HR+/HER-BC are not publicly disclosed yet.

*Source: clinical trials, literature review, Frost & Sullivan analysis*

**AKT Targeting Drug Clinical Data – Other Indications**

| Company | Drug | NCT number | Phase | No. of patients | Indication | Treatment Line | Intervention/ Treatment | Median Follow-up Duration (month) | Median Overall Survival (month) | Median Progression-Free Survival (month) | Objective Response Rate | Adverse Event Rate (≥G3) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Roche | Ipatasertib | NCT01562275 | Ib | 66 | Solid tumors, Expansion in PTEN deficient, TNBC, or endometrial CA | ≥1L | Ipatasertib + Cobimetinib | NA | NA | NA | 5% | NA |
| | | NCT01362374 | I | 122 | Solid tumors | ≥1L | Ipatasertib + A docetaxel; B mFOLFOX6; C paclitaxel; D enzalutamide | NA | NA | NA | NA | A – 77.8% B – 76.5% C – 51.9% D – 44.1% |
| | | NCT01090960 | I | 52 | Solid tumors | ≥2L | Ipatasertib | NA | NA | NA | ORR 0% DCR 34% | Total NA; Grade 3 diarrhea – 17.2% |
| AstraZeneca | Capivasertib | NCT02338622 | I | 56 | Solid Tumors | ≥2L | Capivasertib + Olaparib | NA | NA | NA | 25% | NA |
| | | NCT02208375 | I/II | 30 | TNBC, Ovarian, primary peritoneal, fallopian tube, or Endometrial | ≥1L for metastasis disease; ≥2L for others | Capivasertib + Olaparib | NA | NA | NA | 24% overall; 50% endometrial | NA |
| | | NCT01226316 | I | Part A & B – 90 Part C – 59 | Solid tumors + PIK3CA mutation | ≥2L | Capivasertib | NA | NA | NA | ORR 0%; DCR 30% | Total NA; 20% Hyperglycemia |
| Taiho Oncology | TAS-117 | NCT03017521 | II | 13 | Solid tumors | ≥2L | TAS-117 | 6.6 | 4.8 | 1.4 | 8% | 15% |
| EMD Serono | M2698 | NCT01971515 | I | 101 | Solid tumors | ≥2L | M2698 + tamoxifen | NA | NA | 5.5 | NA | 19% |
| Laekna | LAE002 (Afuresertib) | NCT01476137 | I | 20 | Solid Tumors + Myeloma | ≥1L | Afuresertib + Trametinib | | | | 5% | |
| | | NCT00881946 | I/II | 73 | AML, ALL/CLL, NHL, HL, LCH, MM | ≥2L | Afuresertib | NA | NA | NA | 8.8% (MM) | NA |

*Note:* Information as of April 30, 2023. Only trials with results published by April 30, 2023 were included. Trial data were obtained from the literature and public information, not head-to-head trials, and comparisons are for informational purposes only.

*Source: clinical trials, literature review, Frost & Sullivan analysis*

## *Competitive Advantages*

### *High Potency and Selectivity*

LAE002 is a potent pan-AKT inhibitor that inhibits all three AKT isoforms (AKT1, AKT2 and AKT3). Currently, there are two AKT inhibitors in the late stage clinical development for anti-cancer treatment in China, namely LAE002 and AstraZeneca's capivasertib. The following table sets forth a comparison of potency, PK/PD and *in vivo* efficacy of LAE002, ipatasertib and capivasertib on the inhibition of AKI in the pre-clinical studies. The results shows that LAE002 has a strong potency of AKT inhibition comparable to ipatasertib and capivasertib.

| | LAE002 afuresertib (ATP Competitive) Laekna | GDC-0068 ipatasertib (ATP Competitive) Roche | AZD-5363 capivasertib (ATP Competitive) AstraZeneca |
|---|---|---|---|
| AKT inhibition (IC50) | 0.08 nM (AKT1)<br>1.35 nM (AKT2)<br>16.67 nM (AKT3)<br>0.2 nM (AKT1E17K) | 0.21 nM (AKT1)<br>26.73 nM (AKT2)<br>129.40 nM (AKT3) | 0.25 nM (AKT1)<br>1.38 nM (AKT2)<br>41.59 nM (AKT3) |
| Cellular potency (LNCaP, pPRAS40, IC50) | 237 nM<br>104 nM | 273 nM<br>157 nM | 336 nM<br>220 nM |
| PK/PD (pPRAS40 reduction, xenograft) | @ 100 mg/kg, 60% reduction | @100 mg/kg (~2.6 uM plasma conc), 87% reduction | @ 300 mg/kg, 90% reduction |
| *In vivo* xenograft model efficacy | BT474: 61% TGI @100 mg/kg; HCC1954; >100% TGI @100 mg/kg; SKOV3: 97% TGI @ 100 mg/kg | PC3 xenograft, 79% TGI @ 100 mg/kg | BT474: 39% TGI @ 100 mg/kg, QD; 80% TGI @ 100 mg/kg, BID |

*Note:* No head-to-head comparison clinical study was conducted between the drug candidates above. Clinical trials of a drug cannot be directly compared to the clinical trials of another drug candidates and may not be representative of the overall data.

*Glossary & abbreviation:*

IC50: the concentration where half maximal inhibition is reached; conc: concentration

*Source: Frost & Sullivan analysis, Company data*

In the further investigation of LAE002 inhibition on a broad panel of 49 *in vitro* expressed human protein kinases, LAE002 minimally inhibited 12 other kinases ($IC_{50}$ = 1 to 10 μM) and potently inhibited four additional kinases including: PKA (1.2 nM), ROCK1 (110 nM), p70S6K (200 nM), and RSK (320 nM). When LAE002 was evaluated against a panel of 230 unique kinases in an additional experiment, 0.5 μM LAE002 demonstrated over 50% inhibition of 18 kinases, including, among other, members of the AGC kinase family such as PKA, PKC, and PKG. In a further investigation of the inhibition of the PKC and PKG kinase isoforms, LAE002 inhibited PKG1α, PKG1β, PKCη, PKCβ1, PKCθ and PKC**δ** with $IC_{50}$ values of 0.9, 4.0, 210, 430, 510, and 1,000 nM, respectively. These pre-clinical results support the low off-target activities for LAE002 that have been translated into relatively low rate of adverse events typically reported in other AKT inhibitors clinical trials, such as hyperglycemia, diarrhea, skin rashes, etc.

*Anti-Tumor Efficacy and Favorable Safety Profile*

According to Frost & Sullivan, there are two AKT inhibitors (LAE002 and capivasertib) that have entered registrational clinical trials globally after Roche recently terminated two Phase III clinical trial studies for ipatasertib. As compared with early phase clinical trial results of AstraZeneca's capivasertib and Roche's ipatasertib (which has ongoing Phase II clinical trials but recently terminated all of its Phase III clinical trials), LAE002 demonstrated several advantages, including in potency, tumor inhibition exposure and toxicity, based on public data (not a head-to-head study), as further elaborated in the table below.

| | | **LAE002 afuresertib (ATP Competitive)** | **GDC-0068 ipatasertib (ATP Competitive)** | **AZD-5363 capivasertib (ATP Competitive)** |
|---|---|---|---|---|
| Study Ph1 | | 25, 75, 100, 125, 150 mg QD | 100, 200, 400, 600, 800 mg QD | 80 - 600 mg BID Continued dosing<br>480, 640 mg BID 4d/7d dosing<br>640, 800 mg BID 2d/7d dosing |
| Recommended Ph2 Dose (RP2D) | | 125 mg QD | 600 mg QD | 480 mg BID 4/7 days |
| Cancer Type & Patients Enrolled | | Hematologic tumors<br>73 pts | Solid tumors<br>52 pts<br>(breast cancer – 31%, colorectal cancer – 27%, prostate cancer – 12%, chondrosarcoma – 4%, ovarian cancer – 4%, other – 22%) | Solid tumors<br>Part A & B - 90 pts<br>(colorectal – 29%, pleura – 8%, lung – 7%, cervix – 6%, colon – 6%, other – 45%)<br>Part C – 59 pts<br>(solid tumor patients with PIK3CA mutation) |
| AUC0-24 ng-h/mL /Cmax ng/mL /Ctrough ng/mL | Initial State | AUC 2378/ Cmax 175 | AUC 2670/ Cmax 488 | n/a |
| | Steady State | AUC 7405/Cmax 531/Ctrough259 (Cycle 1 day 8) | AUC 4450/Cmax 748 (Cycle 1 Day 15) | AUC 7952/Cmax 1426/Ctrough 357 (Day 4 on 4/7d) |
| Major Adverse Events @RP2D >= G3 | | <u>G3 (all dose level)</u><br>6.8% Neutropenia<br>4.1% Rash<br>2.7% Odynophagia<br>2.7% Fatigue<br>0% Hyperglycemia | <u>G3</u><br>17.2% Diarrhea<br>3.4% Hyperglycemia<br>3.4% Hyperphosphatemia<br>3.4% Asthenia | <u>G3 & G4</u><br>20% Hyperglycemia<br>12% Diarrhea<br>10% Maculopapular Rash<br>7% Fatigue<br>7% Hypokalemia |
| Efficacy<br>Single Agent | | ORR 8.8%, DCR 63%<br>1 CR, 4 PR, 33 SD all confirmed | ORR not available, DCR 34%<br>16 SD | ORR not available, DCR 30%<br>27 SD<br>ORR 5.6%, in PIK3CA mutation pts |

*Note:* No head-to-head comparison clinical study was conducted between the drug candidates above. Clinical trials of a drug cannot be directly compared to the clinical trials of another drug candidates and may not be representative of the overall data.

In 2021 and 2023, Roche terminated two Phase III studies of ipatasertib, one for breast cancer and the other for prostate cancer, respectively. In the Phase III trial for breast cancer, the combination therapy of ipatasertib and paclitaxel failed to reach its primary endpoint of improvement in progression-free survival and objective response rate. Similarly, the Phase III trial for prostate cancer failed to meet the overall survival endpoint, although the trial met one of the two primary endpoints of radiographic progression-free survival in PTEN loss group at the earlier data release. We believe that the termination of the Phase III clinical trials of ipatasertib will not impact our clinical trials of LAE002 on the following basis: (i) clinical trial designs of LAE002 and the terminated Phase III ipatasertib clinical trials are different in many ways such as in their combination therapy selection, targeted patient population and dosing regimens, which the success of clinical trials depend on. For example, AKT pathway activation tend to occur in cancer patients that have failed multiple lines of treatment of SOCs and AKT inhibitors demonstrated their abilities to reduce AKT activity and enable patients to become "re-sensitized" to originally resistant therapies. Therefore, a clinical trial of an AKT inhibitor designed to be used as a second or later lines of therapy, which is LAE002's case, potentially will have a higher success rate; (ii) LAE002 and ipatasertib are also very different in their properties such as AKT inhibition, absorption, metabolism and PK profile that may lead to different efficacy results, and LAE002 has demonstrated potentially better potency and drug-like properties in non-head-to-head studies as summarized in the table above compared with ipatasertib.

Prior to the termination of Phase III clinical trials of ipatasertib, another AKT inhibitor's (Aeterna Zentaris' perifosine) Phase III development was discontinued for colon cancer and relapsed and refractory multiple myeloma in combination with bortezomib-dexamethasone. In 2012, it was announced that perifosine failed the Phase III clinical trial for treatment of colon cancer because of the lack of significant difference in the primary endpoints, including the median overall survival and median progression free survival between the perifosine treatment group and the placebo group. In 2013, Aeterna Zentaris announced the discontinuation of Phase III clinical trial of perifosine for the treatment of relapsed and refractory multiple myeloma because it was highly unlikely that the study would achieve a significant difference in its primary endpoint for the progression free survival. However, we believe it will not affect our clinical development plan of LAE002 based on the following: (i) LAE002 and perifosine have different mechanisms of action. Perifosine showed anti-proliferation activity *in vitro* and can reduce the level of phosphorylated AKT in cells, but the exact mechanism is not clear. In comparison, LAE002 has a clear mechanism, and is designed and optimized as a specific AKT inhibitor. Our pre-clinical studies also showed that LAE002 can directly inhibit AKT in enzymatic assays, and can strongly arrest the cell cycle in the G1 phase with enhanced cisplatin induced cytotoxicity; (ii) as a specific AKT inhibitor, LAE002 has a much higher selectivity compared with perifosine. Higher selectivity of drug usually leads to two main benefits: (1) a lower dose intake of the drug to achieve its therapeutic effect, and (2) less off-target effect due to less drug bind to undesired target. Thus, higher selectivity of LAE002 on AKT indicates

potentially better therapeutic effects on cancer; (iii) LAE002 has different disease indications compared to periforine, and the failure of perifosine may not have meaningful indicative value in predicting the therapeutic effect of LAE002 in its disease indications. Although we believe the risk of a similar discontinuation is not applicable to our LAE002 combination study because of the aforementioned differences, our development of LAE002 may still be subject to other development risks.

This table includes information summarized from selected Phase I clinical trials conducted for the three AKT inhibitors. We believe the clinical trials selected are the most relevant clinical trials for the purpose of comparison because each of the clinical trials selected used the relevant AKT inhibitor as monotherapy and assessed a wide range of doses despite that they were conducted for different indications. As the first-in-human studies for LAE002, ipatasertib and capivasertib, the ORR and/or other efficacy data listed above from each of such clinical trials were for the whole enrolled patient group of the relevant clinical trial and such data for each cancer type being studied were not available.

*Glossary & abbreviation: Ph: Phase; Pts: patients; Cmax: maximum concentration; Ctrough: trough concentration; DCR: disease control rate*

*Source: Frost & Sullivan analysis, Company data, Spencer et al. 2014, BLOOD 124(14), Saura et al, 2017, Cancer Discovery, Banerji et al, 2018, Clin Cancer Res; 24(9)*

*Synergistic Effects in Combination with Other Therapies*

In several clinical trials, the combination of LAE002 with other therapies also exhibits favorable efficacy results, such as the completed Phase II study of LAE002 in combination with carboplatin and paclitaxel for the treatment of PROC sponsored by Novartis and the registrational Phase II MRCT study of LAE002 in combination with paclitaxel for PROC sponsored by us. For details of efficacy profiles, see "– Summary of Clinical Trial Results" section below.

Phase II clinical studies conducted by multinational companies, including Roche and AstraZeneca, have demonstrated favorable efficacy of their combination therapy of AKT inhibitors (i.e., ipatasertib and capivasertib) in the treatment of HR+/HER2- mBC and TNBC, respectively. We have observed positive preliminary anti-cancer effects with the combination trial of LAE002 plus LAE005 and nab-paclitaxel in TNBC in the Phase I study. Another ongoing combination trial of LAE002 plus estrogen receptor antagonists in HR+/HER2- mBC is expected to achieve comparable clinical efficacy and safety clinical results given LAE002's similar mechanism of action and safety profiles compared with ipatasertib and capivasertib.

### *Summary of Clinical Trial Results*

The following table sets forth an overview of the key clinical studies of LAE002:

| Name of Trial | Trial ID | Sponsor | Site | Design | Study Arm | Status | Competent Authority | Indication | Planned Patient Enrollment | Actual Patient Enrollment |
|---|---|---|---|---|---|---|---|---|---|---|
| Registrational Phase II MRCT study to assess the efficacy and safety of LAE002 plus paclitaxel versus paclitaxel in patients with PROC | NCT04374630 | the Company | U.S. and China | Open-label, randomized, active-controlled trial | Two arms (the combination treatment arm and the paclitaxel treatment arm) for efficacy and safety evaluation | Active, ongoing | FDA and NMPA | PROC | 141 | 144 (As of the Latest Practicable Date) |
| Phase I/II study of LAE002 in combination with carboplatin and paclitaxel in subjects with PROC | NCT01653912 | Novartis | Australia, Russian Federation and United Kingdom | Open-label trial | Single arm of combination treatment (LAE002 + carboplatin + paclitaxel) for safety, tolerability and efficacy evaluation | Completed | FDA | PROC | 59 | 59 (Data cut-off date is July 1, 2015) |
| Phase I/II MRCT study of LAE001/prednisone plus LAE002 in patients with mCRPC following SOC treatment | NCT04060394 | the Company | Phase I: U.S., Phase II: U.S. and South Korea | Open-label trial | Single arm of combination treatment (LAE001/ prednisone + LAE002) for safety and tolerability evaluation | Phase I: completed Phase II: active, ongoing | Phase I: FDA, Phase II: FDA and Ministry of Food and Drug Safety of South Korea | mCRPC following SOC treatment | Phase I: 24; Phase II: 40; | Phase I: 14 (Data cut-off date is February 2021); Phase II: 35 (Enrollment completed in March 2023) |
| Phase I/II clinical trial of LAE002 in combination with sintilimab and chemotherapy for PD-1/PD-L1 resistant solid tumors | NCT05383482 | the Company | China | Open-label trial | Two arms of combination treatment (LAE002 + sintilimab + nab-paclitaxel and LAE002 + sintilimab + docetaxel) for efficacy and safety evaluation | Active, ongoing | NMPA | PD-1/PD-L1 resistant solid tumors | Phase I: 18-42 Phase II: 50-125 | Phase I: 12 (As of the Latest Practicable Date) |
| Phase I/II clinical trial of LAE002 in combination with LAE005 and nab-paclitaxel for TNBC | CTR20210500, CTR20210475 | the Company | China | Open-label, randomized trial | Single arm of combination treatment (LAE002 + LAE005 + nab-paclitaxel) for efficacy and safety evaluation | Active, ongoing | NMPA | TNBC | Phase I: 21 Phase II: 80; | Phase I: 22 (Enrollment completed in March 2023) |
| Phase Ib/III study evaluating efficacy and safety of LAE002 plus fulvestrant in patients with locally advanced or metastatic HR+/HER2- breast cancer | NCT04851613 | the Company | U.S. and China | Phase Ib: open-label trial Phase III: randomized, double-blind, placebo-controlled trial | Single arm of combination treatment (LAE002 + fulvestrant) for efficacy and safety evaluation | Active, ongoing | FDA and NMPA | Locally advanced or metastatic HR+/HER2- breast cancer | Phase Ib: 20 | Phase Ib: 20 (Enrollment completed in April 2023) |

*Registrational Phase II MRCT Study to Assess the Efficacy and Safety of LAE002 Plus Paclitaxel versus Paclitaxel in Patients with PROC Sponsored by us*

Overview. This study is an open-label, randomized, active-controlled registrational Phase II MRCT study to assess the efficacy and safety of LAE002 plus paclitaxel versus paclitaxel in patients with PROC. The primary endpoint is the PFS based on response evaluation criteria in solid tumors. This trial is regulated by the FDA and the NMPA.

Trial design. Approximately 141 patients with PROC are planned to be enrolled and randomized with a 2:1 ratio in an open-label manner to the two arms (94 patients in the combination treatment arm and 47 patients in the paclitaxel treatment arm) for efficacy and safety evaluation. The study will consist of three periods. The first period is a screening period, during which patients are screened for eligibility according to the inclusion and exclusion criteria. The second period is a treatment evaluation period with a randomized, open-label, two-arm parallel design (from starting study treatment until patients have progressive disease, unacceptable toxicity, death, or withdrawal of consent). The PK study will be applied to both the combination treatment and control arms. The third period is a follow-up period.

Trial status. We initiated this study in July 2020. We have enrolled a total of 144 subjects as of the Latest Practicable Date, with 96 in arm 1 (LAE002 plus paclitaxel) and 48 in arm 2 (paclitaxel only). As of the data cut-off date (February 13, 2022), a total of 61 subjects were randomized with 44 subjects having at least two tumor assessments. Among these subjects, 30 were in arm 1 (LAE002 plus paclitaxel), and 14 were in arm 2 (paclitaxel only). This study is currently ongoing and actively recruiting patients.

Safety data. As of the data cut-off date (February 13, 2022), the most severe common adverse events (reported in >= 10% of patients) in both arms were neutrophil count decreased (24.4% vs 33.3%), white blood cell count decreased (19.5% vs 16.7%) and anemia (9.8% vs 11.1%).

Efficacy data. As of the data cut-off date (February 13, 2022), a total of 44 subjects were evaluated for treatment response. There are 30 subjects in arm 1 (LAE002 plus paclitaxel) and 14 subjects in arm 2 (paclitaxel alone), respectively. The ORRs in arm 1 and arm 2 are 33% and 14%, respectively, including two subjects who achieved CR in arm 1, eight and two subjects had confirmed PRs in arm 1 and arm 2, respectively, 15 and nine subjects had SD in arm 1 and arm 2, respectively, and four and two subjects had PD in arm 1 and arm 2, respectively.

*Phase I/II Study of LAE002 in Combination with Carboplatin and Paclitaxel in Subjects with PROC Sponsored by Novartis*

Overview. This study was an open-label, Phase I/II of LAE002 combined with carboplatin and paclitaxel in subjects with platinum-resistant or refractory ovarian cancer. The primary objective of the study was to determine the safety, tolerability and efficacy of the triplet combination. This trial is regulated by the Therapeutic Goods Administration (TGA) in Australia, the Ministry of Health (Minzdrav) in the Russian Federation and the Medicines and Healthcare Products Regulatory Agency in the United Kingdom.

Trial design. This was an open-label study in subjects with ovarian cancer. Phase I was a 3 + 3 dose-escalation to define an MTD with once-daily LAE002 in combination with carboplatin area under curve (AUC) 5 and paclitaxel 175 mg/m$^2$ in an every three-week schedule. Evaluation of available safety data from at least three subjects that had completed three weeks of study was required prior to defining a new dose and starting the next cohort. Phase II was a dose-expansion study and the primary endpoint is ORR.

Trial Status. Novartis initiated this study on November 13, 2012, and completed this study on July 1, 2015. 59 patients were enrolled, including 28 recurrent PROC patients. 29 patients were enrolled in Phase I study, and 30 patients were enrolled in Phase II study.

Safety data. As of the data cut-off date (July 1, 2015), safety data are available for all 59 subjects. All 59 subjects experienced at least one AE related to study treatment, and most AEs were Grade 3 or lower. The blood and lymphatic (37.3%), gastrointestinal (22.0%), and skin (23.7%) system organ classes accounted for most of these higher-Grade TRAEs.

Efficacy data. Of the 28 recurrent PROC subjects enrolled, the ORR shown was 32.1%. PFS was 7.1 months.

*Phase I/II MRCT Study of LAE001/prednisone Plus LAE002 in Patients with mCRPC Following SOC Treatment Sponsored by us*

Overview. The Phase I study evaluates LAE001/prednisone plus LAE002 in patients with mCRPC following SOC treatment (androgen/androgen receptor and chemotherapy). The primary endpoint of the Phase I study is the safety and tolerability of LAE001/prednisone and LAE002 as combination therapies. The Phase I trial is regulated by the FDA.

Trial design. The Phase I trial is a dose-escalation study to identify the recommended Phase II dose (RP2D) of LAE001/prednisone plus LAE002 in mCRPC patients. There are two cohorts in the Phase I study. In Cohort 1, LAE001 (75 mg, BID) plus prednisone (5 mg, BID) and LAE002 (100 mg, QD) will be administered in cycles of 28 days. In Cohort 2, LAE001 (75 mg, BID) plus prednisone (5 mg, BID) and LAE002 (125 mg, QD) will be administered in cycles of 28 days.

Trial status. We initiated the Phase I study in December 2019, and completed the Phase I study in February 2021, when all the primary endpoints were met. A total of 14 subjects were enrolled. Among these subjects, eight were enrolled into cohort 1 (LAE001 75 mg BID + prednisone 5 mg BID + LAE002 100 mg QD), and six were enrolled into cohort 2 (LAE001 75 mg BID + prednisone 5 mg BID + LAE002 125 mg QD). Results from the Phase I study are summarized below. FDA has no objection for us to initiate the Phase II study in the U.S. We also received the IND approval to initiate the Phase II study in South Korea in March 2022. We completed the patient recruitment in both the U.S. and South Korea in March 2023, with 20 patients in the U.S. and 15 patient in South Korea. The Phase II trial is regulated by the FDA and Ministry of Food and Drug Safety of South Korea.

In the Phase II trial, the anti-tumor efficacy of LAE001/prednisone plus LAE002 will be assessed in mCRPC patients who have progressed on, or who are intolerant of, no more than three prior standard treatments for mHSPC, or nmCRPC, or mCRPC, including at least one anti-androgen treatment and no more than one chemotherapy. The patients will be enrolled for the Phase II study to receive LAE001/prednisone plus LAE002 using RP2D established in the Phase I study. The primary endpoint of the Phase II study is the radiological progression-free survival (rPFS) based on the change in tumor per response evaluation criteria in solid tumors and radiological progression-free survival (rPFS) based changes per prostate cancer working group 3 (PCWG3).

Safety data. For the completed Phase I study, Grade 3 or above AEs were reported in 10 (71.4%) subjects, and drug-related Grade 3 and above AEs were reported in five (35.7%) subjects (one subject with mental status change, two subjects with generalized rash, one subject with alanine aminotransferase (ALT)/aspartate transaminase (AST) increased and one subject with thrombocytopenia). The AE of Grade 4 thrombocytopenia was reported in one (7.1%) subject and was related to LAE002. The dose of LAE001 75 mg BID/prednisone 5 mg BID and LAE002 125 mg QD was determined as the RP2D for the Phase II study. In RP2D cohort, four patients reported Grade 3 AEs, among which one was not related with any study treatment. No Grade 4 or Grade 5 AEs reported in RP2D cohort.

Efficacy data. As of the data cut-off date (February 24, 2022), 14 patients received study treatment for the Phase I study. The median and maximum treatment periods without tumor progression of evaluable patients in RP2D cohort are 8.6 and 15.6 months, respectively. Two patients had a prostate-specific antigen (PSA) response. Among five patients with measurable lesions, one achieved PR and two had SDs.

*Phase I/II Clinical Trial of LAE002 in Combination with Sintilimab and Chemotherapy for PD-1/PD-L1 Resistant Solid Tumors Sponsored by us*

Overview. This is a Phase I/II study to evaluate the safety and efficacy of LAE002 in combination with sintilimab and chemotherapy to treat certain PD-1/PD-L1 resistant solid tumor patients in China. The primary endpoint of the Phase I dose-escalation study is MTD and RP2D. The primary endpoint of the Phase II is ORR. This study is regulated by the NMPA.

Trial status. We received IND approval for this study from the NMPA in January 2022. We initiated the Phase I study in June 2022. As of the Latest Practicable Date, 12 patients were enrolled. We plan to complete the Phase I study with preliminary results in the fourth quarter of 2023.

*Phase I/II Clinical Trial of LAE002 in Combination with LAE005 and Nab-Paclitaxel for TNBC Sponsored by us*

Overview. This study is an open-label, randomized parallel Phase I/II clinical trial. Phase I dose-escalation study is to evaluate the safety and efficacy of LAE002 in combination with LAE005 and nab-paclitaxel in advanced solid tumors in China. The Phase II study is to evaluate the safety and efficacy of LAE002 in combination with LAE005 and nab-paclitaxel in locally advanced or metastatic TNBC. The primary endpoint of the Phase I study is MTD and RP2D. The primary endpoint of the Phase II study is ORR. This study is regulated by the NMPA.

Trial Status. We initiated this study in July 2021. The Phase I study completed the patient recruitment in March 2023, with 22 patients enrolled. We plan to obtain the Phase I read-out in the fourth quarter of 2023.

*Phase Ib/III Study Evaluating Efficacy and Safety of LAE002 Plus Fulvestrant in Patients with Locally Advanced or Metastatic HR+/HER2- Breast Cancer Sponsored by us*

Overview. This is a Phase Ib/III study to evaluate the efficacy and safety of the combination therapy with LAE002 plus fulvestrant in patients with HR+/HER2- breast cancer who have failed one to two prior lines of endocrine therapy and CDK4/6 inhibitor (up to 1 therapy), and chemotherapy (up to 1 chemotherapy).

Trial Design. The Phase Ib part is a single-arm, open-label, proof-of-concept study to evaluate anti-tumor efficacy, safety, tolerability and pharmacokinetics of the combination therapy of LAE002 plus fulvestrant. The primary endpoint of the Phase Ib part is the investigator-assessed ORR of the LAE002 plus fulvestrant combination therapy in HR+/HER2- breast cancer. 20 patients will be enrolled in this part. There will be a safety run-in period during the first 28-days of treatment (Cycle 1) of the first six enrolled patients to evaluate the safety of the initial treatment doses. Patients will receive LAE002 125 mg oral administration, QD in combination with fulvestrant 500 mg intramuscular injection on day one and day 15 of Cycle 1, and fulvestrant 500 mg intramuscular injection on day one of each subsequent four-week cycle.

The Phase III part is a multi-center, randomized, double-blind, placebo-controlled registrational study with two parallel treatment arms to further assess the anti-tumor efficacy and safety of LAE002 combined with fulvestrant (experimental arm) versus placebo combined with fulvestrant (control arm) in patients with HR+/HER2- breast cancer who have failed 1 to 2 prior lines of endocrine therapy (ET), and/or CDK4/6 inhibitor (up to 1 therapy), and/or chemotherapy (up to 1 chemotherapy). The primary endpoint of the Phase III part is the investigator-assessed PFS of the experimental arm and control arm. The major secondary endpoints include the OS, ORR, DOR, DCR and safety. A total of 252 patients will be randomized in a 1:1 ratio to the two parallel treatment arms, namely LAE002 plus fulvestrant and placebo plus fulvestrant. The treatment doses of the study will be based on doses and schedule established in the Phase Ib part.

Trial status. We initiated the Phase Ib study in China and the U.S. in May 2022. The clinical trial completed the patient recruitment in April 2023, with 20 patients enrolled.

***Post-Licensing R&D Activities***

In the Phase I/II Study of LAE002 in combination with carboplatin and paclitaxel in patients with PROC sponsored by Novartis, as of the data cut-off date (July 1, 2015), all 59 subjects experienced at least one AE related to study treatment, and most AEs were Grade 3 or lower. The blood and lymphatic (37.3%), gastrointestinal (22.0%), and skin (23.7%) system organ classes accounted for most of these higher-Grade TRAEs. Of the 28 recurrent PROC subjects enrolled, the ORR shown was 32.1% and PFS was 7.1 months. The clinical data obtained by Novartis suggest that LAE002 has a manageable safety and favorable safety profile for solid tumors, consistent with AKT pathway inhibition. Based on Novartis' study, we designed the registrational Phase II MRCT study to assess the efficacy and safety of LAE002 plus paclitaxel versus paclitaxel in patients with PROC. Based on the results of Roche's AKT inhibitor study for mCRPC and AstraZeneca's AKT inhibitor study for breast cancer, we designed clinical studies of LAE002 to evaluate its therapeutic potential on the treatment of mCRPC and breast cancer, respectively. We are also evaluating LAE002's therapeutic potential in PD-1/L1 drug-resistant solid tumors based on the characteristics of AKT pathways.

When we in-licensed LAE002 from Novartis, several clinical trials had been conducted by Novartis to evaluate the safety and efficacy of LAE002. In these trials, LAE002 was generally well-tolerated in patients and exhibited favorable evidence of efficacy. LAE002 was also being evaluated in an ongoing Phase I/II clinical trial combined with carboplatin and paclitaxel in subjects with PROC. Since our in-license of LAE002 from Novartis, we have designed a Phase I/II study of LAE001 and prednisone plus LAE002 or docetaxel/prednisone plus LAE002 in patients with mCRPC following SOC treatment. We have completed the Phase I clinical trial in the U.S. and have initiated the Phase II clinical trial to evaluate LAE002 in combination with other therapies as second-line treatment for varies indications in the U.S. and South Korea. We are also conducting another four clinical trials, please see "– Summary of Clinical Trial Results" section for further details. The trial designs of the clinical studies we conducted were different from Novartis'. For these clinical trials and other trials we have initiated for LAE002, our R&D team as the sole sponsor, is responsible for the formulation of trial design and the preparation and management of trial implementation, including the selection of vendors and clinical sites, preparation of standards of practice, guidelines and other documents, provision of training to investigators, screening and recruitment of patients, follow-up visits, collection, verification and analysis of trial data.

***Licenses, Rights and Obligations***

On May 9, 2018, we entered into a license agreement with Novartis. According to the license agreement, Novartis grants us an exclusive, royalty-bearing, sub-licensable and assignable license regarding the licensed patents and data to develop, use, manufacture or have manufactured and/or commercialize LAE002 in any and all therapeutic, prophylactic and/or diagnostic uses in humans worldwide. For more details, please see "– Collaboration and Licensing Arrangements – Collaboration with Novartis – LAE002 and LAE003 License Agreement" in this section.

***Clinical Development Plan***

We have initiated a global MRCT Phase II registrational trial in both the U.S. and China to treat PROC with LAE002, in a combination therapy with paclitaxel. As of the Latest Practicable Date, we had enrolled 144 subjects in both the U.S. and China. We aim to make NDA submissions to the FDA and NMPA in the fourth quarter of 2023. If the Phase II study cannot fulfil registrational purposes, we will then conduct a randomized, controlled, double blinded Phase III trial or another equivalent trial subject to our clinical trial results and our communication with the NMPA and the FDA.

We initiated the Phase II clinical trial of the Phase I/II MRCT study of LAE001 and prednisone plus LAE002 or docetaxel/prednisone plus LAE002 in patients with mCRPC following SOC treatment in the U.S. in June 2021. We initiated the same study in South Korea in September 2022. We completed the patient recruitment in both the U.S. and South Korea in March 2023. Furthermore, we plan to design a randomized, controlled, double blinded Phase III registrational MRCT or another equivalent MRCT subject to our Phase II clinical trial results and our communication with the NMPA, for the same indication in the U.S., Asia and Europe. We expect to initiate this MRCT in the U.S. first in the second half of 2023 and submit an NDA to the FDA and NMPA in 2025.

In addition, we are also actively exploring to further expand the indication of LAE002. We are collaborating with Innovent in a combination therapy with sintilimab targeting patients with solid tumors with prior PD-1/PD-L1 treatments. We received the IND approval for this Phase I/II study from the NMPA in January 2022 and initiated the Phase I study in June 2022. We plan to complete the Phase I study and the analysis of the preliminary results in the fourth quarter of 2023. We are also conducting a Phase Ib/III trial in China and the U.S. for the treatment of locally advanced or metastatic HR+/HER2- breast cancer with LAE002, in a combination therapy with fulvestrant. The Phase Ib study completed the patient recruitment in April 2023, with 20 patients enrolled. We plan to initiate the MRCT Phase III study including China and the U.S. in the second half of 2023, with top-line results expected to become available in the first half of 2025 and NDA submissions to the FDA and the NMPA in the second half of 2025.

We are aware that a Phase III clinical trial of capvasertib, an AKT kinase inhibitor, has met primary endpoints in HR+ HER2- advanced or metastatic breast cancer. Although capivasertib is taking a randomized, controlled, double blinded approach in its registrational trial, we believe that risk of being requested by the NMPA to modify the design of our clinical trial is low on the following basis: (i) our trial design has already been approved by the NMPA for registrational purpose and is non-inferior to that of capivasertib, and (ii) our preliminary clinical results are favorable and it is highly likely that the endpoints of the Phase Ib/III clinical study will be met without a need to conduct additional studies. As of the Latest Practicable Date, we have not received any NMPA inquiry on requesting us to change the design of our clinical trial because of this update regarding capivasertib. We believe that this will not materially impact our development and commercialization plan for LAE002 as we have taken the advancement of capvasertib's R&D progress into consideration when formulating such a plan for LAE002.

***Material Communications with Competent Authorities***

For the registrational Phase II MRCT study to assess the efficacy and safety of LAE002 plus paclitaxel versus paclitaxel in patients with PROC sponsored by us, we filed an IND application to the FDA in October 2019 and received its approval after its 30-days review. We filed another IND application to the NMPA in June 2020 and received its approval in August 2020. According to the written confirmation issued by FDA in February 2019 and by NMPA in February 2020, FDA and NMPA agreed that this global MRCT Phase II trial would be the registrational trial for the registration purpose, on the basis that: (i) our pre-clinical studies suggest that increased AKT activity could be a primary mechanism of resistance to platinum and taxane therapy, and that resistance can be reversed by AKT inhibitors; and (ii) the preliminary efficacy of paclitaxel, carboplatin and LAE002 combination was observed in PROC patients from previous proof-of-concept clinical studies and the treatment effect of paclitaxel and LAE002 combination was shown in a previous gastric cancer study, our Phase II study is appropriate to support product registration under accelerated approval if our Phase II clinical results can demonstrate an improvement in PFS over SOC considering the poor prognosis of PROC patients with their huge and urgent unmet medical needs for new treatments.

For the Phase I/II MRCT study of LAE001 and prednisone plus LAE002 or docetaxel/prednisone plus LAE002 in patients with mCRPC following SOC treatment sponsored by us, we filed an IND application to the FDA for Phase I/II study in May 2019 and received its approval after its 30-days review. We completed the Phase I study in February 2021. FDA has no objection for us to initiate the Phase II MRCT study of LAE001 and prednisone plus LAE002 or docetaxel/prednisone plus LAE002 in patients with mCRPC following SOC treatment in the U.S.. We received another approval from Ministry of Food and Drug Safety of South Korea to initiate a Phase II study of LAE001 and prednisone plus LAE002 or docetaxel/prednisone plus LAE002 in patients with mCRPC following SOC treatment in South Korea in March 2022.

For the Phase I/II study of LAE002 combined with sintilimab for PD-1/PD-L1 resistant solid tumors sponsored by us, we filed an IND application in terms of the trial design for the above study to the NMPA in November 2021, and subsequently, in January 2022, we received its IND approval from the NMPA.

For the Phase I/II study of LAE002 combined with LAE005 and nab-paclitaxel for TNBC sponsored by us, we filed an IND application in October 2020, we received its IND approval from the NMPA in December 2020.

For the Phase Ib/III study evaluating efficacy and safety of LAE002 plus fulvestrant in patients with locally advanced or metastatic HR+/HER2- breast cancer sponsored by us, we filed an IND application to FDA in May 2021. FDA has approved this study after its 30-day review. We also filed this IND for MRCT to the NMPA in June 2021 and received its IND approval from the NMPA in August 2021.

We had not received any relevant regulatory agency's concerns or objections to our clinical development plans as of the Latest Practicable Date, nor did any material unexpected or adverse changes had occurred since the date of issue of relevant regulatory approvals for LAE002.

## WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET LAE002 SUCCESSFULLY.

### Core Product LAE001: A Dual CYP17A1/CYP11B2 Inhibitor

***Overview***

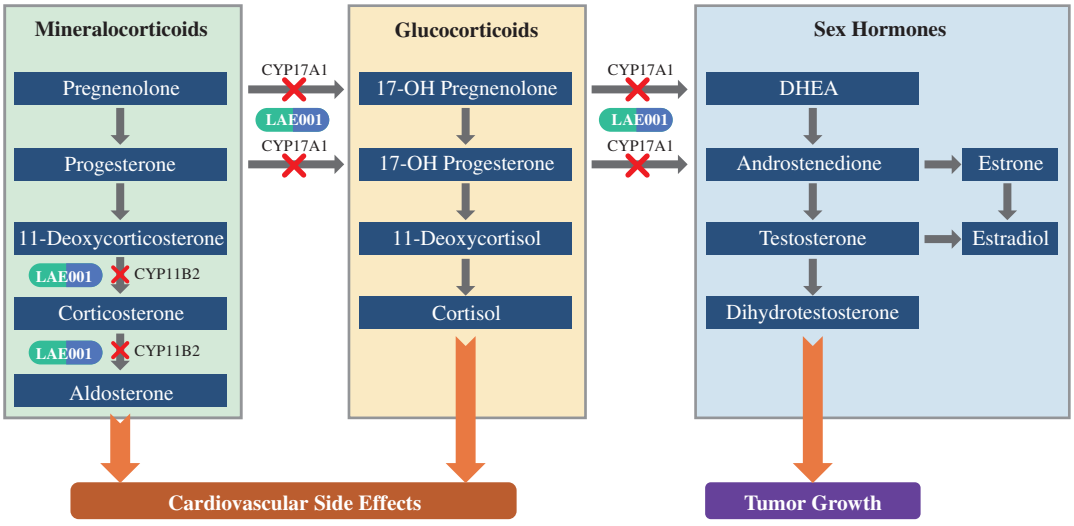
LAE001 is an androgen synthesis inhibitor that inhibits both CYP17A1 and CYP11B2. We in-licensed LAE001 from Novartis in 2017. According to Frost & Sullivan, LAE001 is the only dual CYP17A1/CYP11B2 inhibitor in clinical trials for the treatment of prostate cancer globally. As a dual CYP17A1/CYP11B2 inhibitor, LAE001 can block both androgen and aldosterone synthesis and potentially be administrated without prednisone, the short-term high dose or long-term exposure of which can lead to a variety of adverse events. Our completed Phase I study showed safety, preliminary anti-tumor efficacy and clinical benefits in mCRPC patients. We are currently conducting a Phase II clinical trial of LAE001 monotherapy on mCRPC. As part of our clinical development strategy for LAE001 in prostate cancer and based on the clinical data from trials on mCRPC, we plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S. and apply the NDA for mHSPC with the NMPA and the FDA in 2027.

***Mechanism of Action***

Androgens are closely related to the growth of the prostate and the occurrence of prostate cancer. Therefore, endocrine therapy has become an effective treatment for prostate cancer. Endocrine therapy includes estrogen therapy, gonadotropin-releasing hormone analog therapy, gonadotropin – releasing hormone antagonist therapy, and androgen suppressive therapy, among which the androgen suppressive therapy can be used alone for the treatment of early-stage prostate cancer or combined with surgery for adjuvant therapy. Androgen therapy is one of the main methods of clinical treatment of prostate cancer, which involves the intervention of the androgen signaling pathway. CYP11B2 enzyme is one of the enzymes in the steroidogenesis pathway and is responsible for the catalysis of last three steps in the aldosterone biosynthetic cascade. It is encoded by the CYP11B2 gene located on human chromosome 8q21-22. The genetic element of cardiovascular disorders has emerged as a risk factor for the progression of these disorders. Among these genetic elements, CYP11B2 genetic variants and haplotypes play a registrational role in the susceptibility, progression, survival, and therapeutic response of many cardiovascular disorders such as hypertension, coronary heart disease, atrial fibrillation, cardiomyopathy, heart failure, and other disorders.

Abiraterone, a CYP17A1 enzyme inhibitor, can block the synthesis of androgens to improve patients' survival in both mCRPC and mHSPC. Abiraterone acetate, a CYP17A1 enzyme inhibitor, is currently approved only for use in combination with prednisone. Depending on the length of usage and dosage, prednisone may cause adverse events. Cumulative doses of prednisone administered over a long period of time or from high doses even for a short-term exposure may cause altered bone metabolism, immunosuppression, increased risk of hyperglycemia and diabetes mellitus, hepatotoxicity, decreases in mood and cognitive function, and muscle weakness. LAE001, a dual inhibitor of CYP17A1 and CYP11B2 (aldosterone synthase), can block both androgen and aldosterone synthesis and potentially being administrated without prednisone, and thereby reduce prednisone-related side effects.

The following diagram illustrates the mechanism of action of LAE001:




*Glossary & abbreviation:*

DHEA: dehydroepiandrosterone

*Source: Company data*

### *Market Opportunity and Competition*

*Market Opportunities of LAE001 for mHSPC*

According to Frost & Sullivan, the global and China incidence of prostate cancer is expected to increase from 1,451.5 thousand and 120.9 thousand in 2021 to 1,815.1 thousand and 199.3 thousand in 2030, respectively. Patients with prostate cancer that have relapsed after local therapy or that have distant metastasis usually respond to androgen deprivation therapy (ADT). HSPC is the stage of prostate cancer where the patients effectively respond to hormone therapies, typically ADT. The current SOC for mHSPC consists mainly of chemotherapies and anti-androgen therapies including abiraterone acetate and enzalutamide. However, both abiraterone acetate and enzalutamide have long-term side effects and almost all mHSPC patients eventually develop acquired resistance, leaving no effective treatment options.

As abiraterone is a CYP17A1 enzyme inhibitor that cannot address CYP11B2 enzyme, it requires co-medication with corticosteroids or GnRH analogs to manage adverse effects. In comparison, LAE001 has exhibited its high potency and selectivity against both the CYP17A1 and CYP11B2 enzymes in the pre-clinical studies. The CYP11B2 inhibitory activity of LAE001 could potentially reduce the mineralocorticoid excess effects observed with abiraterone by reducing plasma aldosterone levels. Currently, our clinical results demonstrated LAE001's therapeutic potential for the treatment of mCRPC. We plan to initiate a Phase III MRCT registrational trial of LAE001 for mHSPC in the fourth quarter of 2023 in China and the U.S., and submit NDA for LAE001 for the indication of mHSPC to the FDA and NMPA in 2027.

*Competitive Landscape*

According to Frost & Sullivan, currently, there is only one CYP17A1 inhibitor approved for commercialization globally, namely abiraterone. There are 11 anti-androgen drugs in clinical trials globally and LAE001 is the only CYP17A1 and CYP11B2 inhibitor under clinical development. In China, there are five anti-androgen drugs in clinical trials and LAE001 is the only CYP17A1 inhibitor in clinical trial stage.

**Marketed Anti -androgen Drug in the US and China**

| Approved drug | Flutamide | Bicalutamide | Nilutamide | Abiraterone | Enzalutamide | Apalutamide | Darolutamide | Rezvilutamide |
|---|---|---|---|---|---|---|---|---|
| Commercial name | Fugerel | Casodex | Nilandron | Zytiga | Xtandi | Erleada | Nubeqa | 艾瑞恩 |
| Mechanism | AR inhibitor | AR inhibitor | AR inhibitor | CYP17A1 inhibitor | AR inhibitor | AR inhibitor | AR inhibitor | AR inhibitor |
| Company | Ferring | Astra Zeneca | Concordia | Janssen Biotech | Astellas | Janssen Biotech | Bayer | Hengrui Medicine |
| US approval time | 1989* | 1995 | 1996 | 2011 | 2012 | 2018 | 2019 | Not approved |
| 2020 global revenue (million US dollar) | NA | 388.3 | NA | 2,767.6 | 5,134.3 | 760.0 | 317.0 | NA |
| 2022 US market price (US dollar) | NA | 115.0 (50mg) | 285.8 (150mg) | 94.8 (250mg) | 113.8 (40mg) | 117.8 (60mg) | 106.7 (300mg) | NA |
| 2022 US monthly treatment cost (thousand US dollar) | NA | 3.5 (PFS:NA) | 3.5 (PFS:21.1) | 11.4 (PFS:NA) | 13.6 (mCRPC PFS:19.5 nmCRPC PFS:36.6 mHSPC PFS:NA) | 14.1 (mHSPC PFS:NA nmCRPC PFS:40.5) | 12.8 (PFS:40.4) | NA |
| FDA approved indications | B2-C stage prostate cancer, D2 stage metastasis prostate cancer | Metastatic prostate cancer | Metastatic prostate cancer | mCRPC, HSPC | CRPC, mHSPC | mHSPC, nmCRPC | nmCRPC, mHSPC | NA |
| China approval time | 2003 | 1999 | Not approved | 2015 | 2019 | 2019 | 2021 | 2022 |
| NMPA approved indications | Prostate cancer | Late stage Prostate cancer | NA | mCRPC, mHSPC | mCRPC, nmCRPC | nmCRPC, mHSPC | nmCRPC, mHSPC | mHSPC |
| China NRDL inclusion | Category B | Category B | NA | Category B | Category B | Category B | Category B | Category B |
| China generic drug approval status | Y | Y | NA | Y | Y | N | N | N |
| 2020 China revenue (million RMB) | 20.5 | 776.6 | NA | 1,614.3 | 141.5 | 38.9 | NA | NA |
| 2021 China market price (RMB) | NA | 31.0 (50mg) | NA | 108.5 (250mg) | 69.6 (40mg) | 332.5 (60mg) | 196.7 (300mg) | NA |
| 2021 China generic drug market price (RMB) | 3.8 (250mg) | 25.0 (50mg) | NA | 30.0 (250mg) | 48.2 (40mg) | NA | NA | NA |
| 2021 China monthly treatment cost (thousand RMB) | NA | 0.9 (PFS:NA) | NA | 13.0 (PFS:NA) | 8.4 (mCRPC PFS:19.5 nmCRPC PFS:36.6) | 39.9 (mHSPC PFS:NA nmCRPC PFS:40.5) | 23.6 (PFS:40.4) | NA |
| 2021 China generic drug monthly treatment cost (thousand RMB) | 0.3 (PFS:NA) | 0.8 (PFS:NA) | NA | 3.6 (PFS:NA) | 5.8 (mCRPC PFS:19.5 nmCRPC PFS:36.6) | NA | NA | NA |

*Notes:*

1. There were over 15 generic competitors of the approved anti-androgen drugs as of April 30, 2023. If the generic name of a drug is listed in the NRDL, both the original drug and the generics under such generic name will be included in the NRDL and available for reimbursement. Once a drug is included in the NRDL, it will be subject to volume-based purchasing in China.

2. Revenue includes revenue from both the original drug and generics.

3. The chart does not include ADT drugs.

4. Information as of April 30, 2023.

*Source: NMPA, FDA, Frost & Sullivan analysis*

**Pipeline global**

| Drug name | Target | Company | Indication | Phase | First posted date |
|---|---|---|---|---|---|
| SHR3680 | AR inhibitor | Hengrui Medicine | HSPC, mCRPC, advanced breast cancer | III | 2018-05-09 |
| HC-1119 | AR inhibitor | Hinova Pharmaceuticals | mCRPC | III | 2019-02-22 |
| Seviteronel/VT-464 | Dual CYP17A1 and AR inhibitor | Innocrin Pharmaceuticals | CRPC, HR+ breast cancer, TNBC | II | 2013-12-17 |
| Proxalutamide/GT0918 | AR inhibitor | Kintor Pharma | mCRPC | II | 2019-04-02 |
| TRC253 | AR inhibitor | Tracon | mCRPC | I/II | 2016-12-09 |
| ODM-208 | CYP11A1 | Orion Corporation/Merck | mCRPC | I/II | 2018-02-19 |
| **LAE001** | **Dual CYP17A1 and CYP11B2 inhibitor** | **Laekna** | **mHSPC*** | **II** | **2019-02-18** |
| ODM-209 | CYP11A1 | Orion Corporation | Metastatic/advanced prostate cancer, metastatic/advanced breast cancer | I/II | 2019-03-18 |
| EPI-7386 | AR inhibitor | ESSA Pharmaceuticals | mCRPC | I/II | 2021-10-13 |
| TAS3681 | AR inhibitor | Taiho Oncology | mCRPC | I | 2015-10-02 |
| ONC1-0013B | AR inhibitor | Avionco LLC | mCRPC | I | 2017-03-03 |

*Note:* Only includes oncology drugs. The chart does not include androgen deprivation therapy (ADT) drugs or PROTAC. First posted date denotes the date when the most advanced clinical stage of a clinical trial for an indication is first publicly announced. Information as of April 30, 2023.

* We are currently conducting a Phase II clinical trial of LAE001 monotherapy on mCRPC. As part of our clinical development strategy for LAE001 in prostate cancer and based on the clinical data from trials on mCRPC, we plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S. and submit the NDA for mHSPC.

**Pipeline in China**

| Drug name | Mechanism/Target | Company | Indication | Phase | First posted date |
|---|---|---|---|---|---|
| Proxalutamide | AR inhibitor | Kintor Pharma | mCRPC | III | 2018-07-02 |
| HC-1119 | AR inhibitor | Hinova Pharmaceuticals | mCRPC | III | 2019-03-01 |
| ISIS560131/AZD5312 | AR inhibitor | Pyramid Laboratories | AR-V7 positive mCRPC | II | 2021-04-29 |
| **LAE001** | **Dual CYP17A1 and CYP11B2 inhibitor** | **Laekna** | **mHSPC*** | **II** | **2019-04-25** |
| TQB3720 | AR inhibitor | Chia Tai-Tianqing Pharmaceutical | mCRPC | I | 2021-01-26 |

*Note:* Only includes oncology drugs. First posted date denotes the date when the most advanced clinical stage of a clinical trial for an indication is first publicly announced. The chart does not include ADT drugs or PROTAC. Information as of April 30, 2023.

* We are currently conducting a Phase II clinical trial of LAE001 monotherapy on mCRPC. As part of our clinical development strategy for LAE001 in prostate cancer and based on the clinical data from trials on mCRPC, we plan to initiate a Phase III MRCT registrational trial for mHSPC in the fourth quarter of 2023 in China and the U.S. and apply the NDA for mHSPC.

*Source: Global trials referenced ClinicalTrials.gov, Global trials referenced CDE, Frost & Sullivan analysis*

### *Competitive Advantages*

*High Potency and Selectivity*

LAE001 is a highly potent and reversible inhibitor of CYP17A1 and CYP11B2 enzymes. It inhibits CYP17A1 from several species, and acts against the recombinant human enzyme with potency comparable to that of abiraterone based on public data. Moreover, abiraterone is a steroidal irreversible CYP17A1 inhibitor that does not inhibit CYP11B2. LAE001 inhibits both the 17α-hydroxylase and the 17, 20-lyase activity of CYP17A1 equally, thus reducing both plasma androgens and cortisol levels like aldosterone. Also, the CYP11B2 inhibitory activity of LAE001 could potentially reduce the mineralocorticoid excess effects observed with abiraterone by reducing plasma aldosterone levels. Furthermore, because LAE001 has a high selectivity for CYP enzymes (3A4, 2C9, 2D6), it is a better combination partner compared to abiraterone.

*Favorable Safety and Efficacy Profile for the Treatment of mCRPC*

We demonstrated the efficacy of monotherapy of LAE001 for mCRPC after in-licensing. LAE001 monotherapy demonstrated favorable safety profile in avoiding hyperaldosteronism associated symptoms which appeared as adverse events in the combination therapy of abiraterone and prednisone. Depending on the length of usage and dosage, prednisone may cause adverse events. Cumulative doses administered over a long period of time or from high doses even for a short-term exposure to prednisone may cause altered bone metabolism, immunosuppression, increased risk of hyperglycemia and diabetes mellitus, hepatotoxicity, decreases in mood and cognitive function, and muscle weakness. The table below sets forth the clinical results of abiraterone and LAE001 for the treatment of mCRPC. Although they were not head-to-head analyses, we believe that valuable insight can nonetheless be drawn from the comparison of our LAE001 with the abiraterone therapies.

| Trial ID and phase | NCT00473512 Phase II | NCT00474383 Phase II | NCT00485303 Phase II | NCT03843918 Phase I |
|---|---|---|---|---|
| **Study treatment** | Abi+Dexamethasone | Abi+Prednisone/ Prednisolone | Abi+Prednisone/ Prednisolone | LAE001 |
| **Patients (n)** | 42 | 47 | 58 | 20 |
| **Prior treatment** | | | | |
| Abi/Enza naïve | Yes | Yes | Yes | Yes |
| Docetaxel naïve | Yes | No (all 47 patients failed docetaxel) | No (all 58 patients failed docetaxel) | No (4/20 patients failed docetaxel) |
| **Median time to PSA progression (months)** | 7.4 | 5.6 | 5.6 | 12.9 |
| **PSA response** | | | | |
| >50% from baseline | 67% | 51% | 36% | 80% |
| >90% from baseline | 19% | 15% | 16% | 60% |
| **Major AEs** | Hypokalemia, hypertension, fluid overload, and migrainous headaches | Hypertension, hypokalemia, edema, hyperglycemia | Fatigue, dyspnea, AST/ALT elevation | Thrombocytopenia, hypokalemia, hypertension |

*Note:* No head-to-head comparison clinical study was conducted between drugs. Clinical trials of a drug cannot be directly compared to the clinical trials of another drug and may not be representative of the overall data.

Abi: abiraterone; Enza: enzalutamide; AST: aspartate transaminase; ALT: alanine aminotransferase

*Source: Company data G Attard, et al. 2009; AHM Reid, et al. 2010; AC Danila et al. 2010*

### *Summary of Clinical Trial Results*

The following table sets forth an overview of the key clinical studies of LAE001:

| Name of Trial | Trial ID | Sponsor | Site | Design | Study Arm | Status | Competent Authority | Indication | Planned Patient Enrollment | Actual Patient Enrollment |
|---|---|---|---|---|---|---|---|---|---|---|
| Phase I/II clinical trial of LAE001 for mCRPC | NCT03843918 | the Company | China | Open-label trial | Phase I: Single arm of LAE001 monotherapy treatment for safety and tolerability evaluation | Phase I: completed; Phase II: ongoing | NMPA | mCRPC | Phase I: 31; Phase II: 40 | Phase I: 31 (Data cut-off date is January 15, 2022) Phase II: Two (As of the Latest Practicable Date) |
| Phase I clinical trial of LAE001 co-administered with prednisone for mCRPC | NCT01647789 | Novartis | U.S., Belgium, Canada and Spain | Open-label trial | Single arm of combination treatment (LAE001 + prednisone) for efficacy and safety evaluation | Phase I: completed; | FDA, Belgian Federal Agency for Medicines and Health Products, Department of Health of Canada, Spanish Agency of Medicines and Medical Devices | mCRPC | 74 | 31 (Data cut-off date is February 3, 2016) |

*Phase I/II Clinical Trial of LAE001 for mCRPC Sponsored by us in China*

Overview. This study was a Phase I/II study of treating patients with mCRPC in China. The objective of the Phase I study is to study the safety and tolerability of LAE001 monotherapy in patients with mCRPC and determine the MTD and the RP2D of the drug. The Phase I and the Phase II part of the Phase I/II clinical trials are separate and standalone trials. The Phase I study includes Phase Ia study and Phase Ib study. The primary endpoint of Phase Ia study is the frequency and severity of adverse events, including dose-limiting toxicities (DLT). The primary endpoint of Phase Ib study is the PSA response rate. The primary endpoint of Phase II study is to determine proportion of subjects with prostate specific antigen decreasing by more than 50% after treatment. The results of the Phase I study suggested that

the use of LAE001 monotherapy was sufficient for the treatment of mCRPC without the use of prednisone as the results demonstrated better efficacy measured using PSA response compared with the results of the Phase I clinical trial of LAE001 with prednisone for mCRPC sponsored by Novartis.

Trial design. The Phase I study is a dose-escalation study in patients with mCRPC who have never received chemotherapy or who have received chemotherapy (chemotherapy failure or intolerance) and preferentially enrolls patients who had failed chemotherapy. Since the SOC of mCRPC is chemotherapy and androgen/androgen receptor, the market potential of LAE001 as the first-line treatment would be better demonstrated if chemotherapy-naïve patients treated with LAE001 showed good outcomes. Phase Ia is a dose-escalation study to determine the RP2D level of LAE001 in mCRPC patients, whereas the Phase Ib study serves with the purpose of a proof of concept study for safety and anti-cancer efficacy of LAE001 monotherapy in mCRPC patients. The initial dose proposed for the Phase Ia study is 50 mg BID, and the escalated doses are 75 mg BID, 100 mg BID and 125 mg BID, respectively. The dose for the Phase Ib study is 50 mg BID. RP2D will be determined based on a comprehensive analysis of the safety, PK, PD and efficacy data of dose escalation. The dose for the Phase II study is to use the RP2D determined in the Phase I clinical trial. The Phase II study is a single-arm trial based on androgen deprivation therapy treatment with the primary objective of assessing the efficacy and safety of LAE001 in mCRPC patients. The Phase II study plans to enroll approximately 40 patients.

Trial status. We initiated the Phase I trial in May 2019, and completed the Phase I study on September 13, 2021. 17 subjects were enrolled in the dose-escalation Phase Ia (50 mg, 75 mg, 100 mg, and 125 mg), and the dose of 50 mg BID has been selected as the RP2D. Additional 14 subjects were enrolled in the dose-expansion Phase Ib (RP2D: 50 mg). The Phase I clinical trial has been completed (all the primary endpoints of the Phase Ia and Ib studies have been met) and we have initiated the Phase II study to further evaluate the safety and efficacy in mCRPC patient.

Safety data. As of the data cut-off date (January 15, 2022), the most common AEs were hypokalemia, hyperglycemia, anemia, hypertension, edema peripheral, platelet count decreased, aspartate aminotransferase increased, and electrocardiogram QT prolonged. Hypokalemia was reported in 26 (83.9%) subjects, and all were suspected to be related to LAE001. Hyperglycemia was reported in 15 (48.4%) subjects, and all were Grade 1, three of which were unrelated to LAE001. Anemia was observed in 12 (38.7%) subjects, and all were Grade 1 or 2, five of which were unrelated to LAE001. Hypertension was observed in 10 (32.2%) subjects, nine of which were suspected to be related to LAE001, and one subject with Grade 3 hypertension was unrelated to LAE001.

Efficacy data. As of the data cut-off date of January 15, 2022, among 27 evaluable patients, 20 patients (74%) achieved over 50% reduction in PSA response and 14 patients (52%) achieved over 90% reduction in PSA response. In the 50 mg BID RP2D Cohort, among 20 evaluable patients, 16 patients (80%) achieved over 50% reduction in PSA response and 12 patients (60%) achieved over 90% reduction in PSA response.

*Phase I Clinical Trial of LAE001 Co-Administered with Prednisone for mCRPC Sponsored by Novartis*

Overview. This was an open-label, multi-center Phase I study in adult patients with mCRPC. The primary objective of the Phase I study was to estimate the MTD or RP2D of oral LAE001 when co-administered with prednisone to adult patients with mCRPC.

Trial design. Patients in the Phase I dose-escalation study were to continuously receive daily dosing of oral LAE001 capsule co-administered with prednisone twice daily for 28 days (4-week) cycles, with no breaks between cycles. The initial dose of LAE001 was 50 mg BID co-administered with 5 mg BID of prednisone for 28-day cycles. Dose escalation continued until the MTD or RP2D was estimated.

Trial status. Novartis initiated the trial on December 4, 2012, and completed the Phase I study on February 3, 2016. 31 patients were enrolled and treated in the Phase I dose-escalation study.

Safety data. The most commonly reported AE included general disorders and administration site conditions (67.7%), gastrointestinal disorders (67.7%), investigations (64.5%), musculoskeletal and connective tissue disorders (61.3%), and metabolism and nutrition disorders (51.6%). Overall, 24 patients (77.4%) had Grade 3/4 AEs and 11 patients (35.5%) had Grade 3/4 AEs suspected to be related to study drug. The most frequently reported Grade 3/4 AEs suspected to be related to the study drug included thrombocytopenia (five patients; 16.1%), platelet count decreased (three patients; 9.7%), hyponatremia (two patients; 6.5%), and hyperkalemia (two patients; 6.5%). The Grade 3/4 AEs were generally manageable by using adjusted or temporarily interrupted drug dosage, concomitant medication, and/or hospitalization or prolonged hospitalization.

Efficacy data. Overall, four patients in 200 mg BID, two patients in 100 mg BID, one patient each in 50 mg and 150 mg BID treatment arms had over 50% reduction in PSA compared to baseline, at or after 12 weeks of treatment. The median best percentage change in PSA from baseline was higher in the 50 mg BID arm (-27.6%), followed by the 200 mg BID arm (-11.9%) and 100 mg BID arm (-10.7%). RP2D of LAE001 was determined to be 100 mg BID.

***Clinical Development Plan***

We completed the Phase I clinical trial and initiated the Phase II clinical trial of a Phase I/II study in China to assess the safety and efficacy of LAE001 as a monotherapy at recommended Phase II dose (RP2D) in mCRPC. We expect to complete the Phase II study in China with preliminary results in the third quarter of 2023. We plan to initiate a randomized, controlled, double blinded Phase III trial or another equivalent MRCT for mHSPC in the fourth quarter of 2023 in China and the U.S. by leveraging the clinical trial results from the Phase I/II study of LAE001 monotherapy in mCRPC in China following a common development strategy of anti-androgen therapy for prostate cancer since (i) anti-androgen therapy plays an anti-tumor

role by blocking the synthesis of androgens for both mCRPC and mHSPC patients with the same mechanism of action, (ii) mCRPC and mHSPC are late stage and early stage of prostate cancer, respectively, and if the efficacy and safety of the drug are well established in mCRPC patients, it will likely be effective in treating mHSPC patients, (iii) patients with mCRPC have limited treatment options thus mCRPC is more suitable for early phase clinical study in terms of patient enrollment, and (iv) the treatment effect in mCRPC patients could be observed in a short follow-up period compared with mHSPC patients because mCRPC patient is in a later stage of cancer with shorter life expectation length, thereby shortening drug development time. We will apply the NDA for mHSPC with the NMPA and the FDA in 2027.

***Post-Licensing R&D Activities***

In the Phase I clinical trial of LAE001 co-administered with prednisone for mCRPC sponsored by Novartis, 24 patients (77.4%) had Grade 3/4 AEs. The most frequently reported Grade 3/4 AEs suspected to be related to the study drug included thrombocytopenia (five patients; 16.1%), platelet count decreased (three patients; 9.7%), hyponatremia (two patients; 6.5%), and hyperkalemia (two patients; 6.5%). Four patients in 200 mg BID, two patients in 100 mg BID, one patient each in 50 mg and 150 mg BID treatment arms had over 50% reduction in PSA compared to baseline, at or after 12 weeks of treatment. The clinical data obtained by Novartis suggest that LAE001 has a manageable safety profile. The efficacy data also suggests LAE001 has a favorable efficacy profile for the treatment of prostate cancer. Based on Novartis' clinical results, we designed the clinical study of LAE001 monotherapy for PROC because of its additional activity on CYP11B2. We expect the overall side effects to be significantly improved over abiraterone acetate or prednisone, while maintaining a similar or even better efficacy against prostate cancer.

When we in-licensed LAE001 from Novartis, a number of clinical trials had been conducted by Novartis to evaluate the safety and efficacy of LAE001. Among these trials, LAE001 was generally well-tolerated in patients and showed evidence of efficacy. In particular, Novartis has completed a Phase I clinical trial in combination with prednisone for the treatment of mCRPC. After the in-licensing, we redesigned a Phase I/II clinical trial to demonstrate the efficacy of monotherapy of LAE001 for mCRPC. The trial design of the clinical study we conducted was different from Novartis'. We completed the Phase I clinical trial and initiated the Phase II clinical trial in China to access safety and efficacy at RP2D of LAE001 in mCRPC as a monotherapy. Compared with the Phase I clinical trial of LAE001 with prednisone for mCRPC sponsored by Novartis, our LAE001 monotherapy clinical trial demonstrated better efficacy in PSA response with manageable side effects, suggesting that LAE001 monotherapy is sufficient for the treatment of mCRPC without the use of prednisone. We also designed and completed a Phase I dose-escalation and efficacy study of LAE001 and prednisone plus LAE002 or docetaxel/prednisone plus LAE002 in patients with mCRPC following the SOC treatment. We conducted clinical activities including (i) preparing the clinical trial design/framework and protocol; (ii) coordinating with the FDA for the review and

approval of our clinical trial, (iii) coordinating all post-licensing clinical development activities, (iv) designing and coordinating the selection process for qualified CROs to assist in engaging clinical sites and coordinating clinical studies once commenced; and (v) supervising the clinical studies.

***Licenses, Rights and Obligations***

On June 30, 2017, we entered into a license agreement with Novartis. According to the license agreement, Novartis grants us an exclusive, royalty-bearing, sub-licensable and assignable license regarding the licensed patent and data to develop, use, manufacture or have manufactured and/or commercialize LAE001 in any and all therapeutic, prophylactic and/or diagnostic uses in humans worldwide. For more details, please see "– Collaboration and Licensing Arrangements – Collaboration with Novartis – LAE001 License Agreement" in this section.

***Material Communications with Competent Authorities***

For LAE001, we filed an IND application for Phase I/II clinical trial of LAE001 for mCRPC to the NMPA in October 2018 and obtained its IND approvals in January 2019. We completed the Phase I study and received the NMPA's approval to initiate the Phase II trial for the treatment of mCRPC in September 2021. We will further consult with the NMPA and obtain their approval before initiating Phase III trials for the treatment of mHSPC.

Based on the IND approval and our ongoing communications with the NMPA, we had not received any relevant regulatory agency's concerns or objections to our clinical development plans as of the Latest Practicable Date, nor had any material unexpected or adverse changes occurred since the date of issue of relevant regulatory approvals for LAE001.

**WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET LAE001 SUCCESSFULLY.**

**LAE005: A Potentially High-Affinity, Ligand-Blocking, Humanized Anti-PD-L1 IgG4 Antibody**

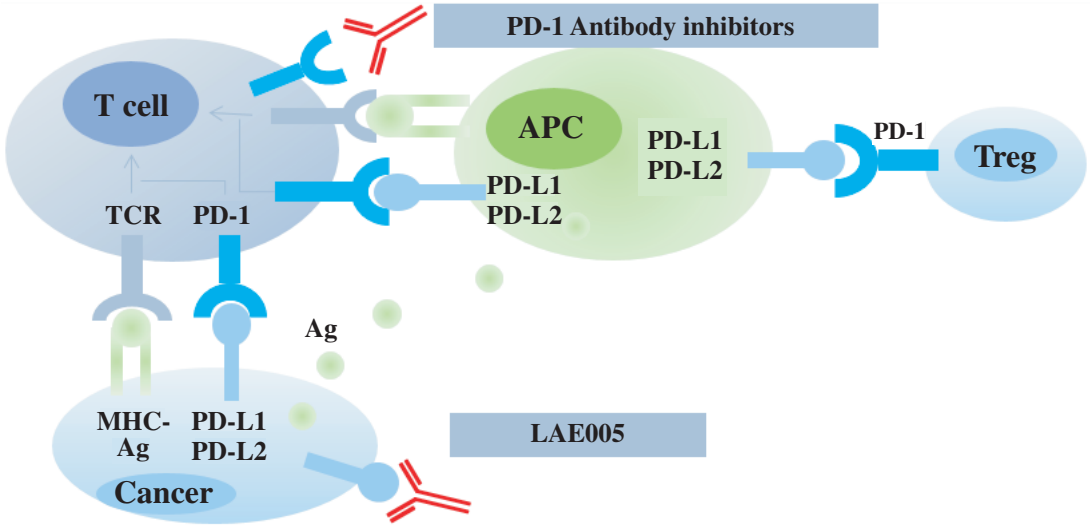
***Overview***

LAE005 is expected to be a high-affinity, ligand-blocking, humanized anti-PD-L1 IgG4 antibody. In the pre-clinical and clinical studies, LAE005 demonstrated its strong binding avidity to PD-L1 and compelling anti-tumor activities. Specifically, we are evaluating the therapeutic potential of the combination therapy of LAE002 and LAE005 in patients with TNBC. We believe LAE005 has the potential to serve as an effective therapy for the treatment of TNBC when combined with other synergistic mechanisms.

### *Mechanism of Action*

Programmed death-1 (PD-1) is a critical immune checkpoint receptor expressed on T cells upon activation. Engagement of PD-1 by its ligands, PD-L1 and PD-L2, transduces a signal that inhibits T-cell proliferation, cytokine production, and cytolytic function. During tumorigenesis, cancer cells from a wide range of tumor types exploit immune checkpoint pathways, such as PD-1/PD-L1, to avoid detection by the adaptive immune system. Monoclonal antibody (mAb) inhibitors of immunological and their corresponding ligands, including PD-1 and PD-L1, have demonstrated significant anti-tumor activity in patients with various solid tumors. LAE005 specifically binds to PD-L1 and likely leads to PD-L1 dimerization, conformational changes, and internalization from cell surface, making PD-1 no longer able to bind to PD-L1 and activate downstream signaling T-cell suppression.

The following diagram illustrates the mechanism of action of LAE005:




*Glossary & abbreviation:*

PD-L2: programmed death ligand-2; TCR: T-cell receptor; APC: antigen-presenting cell; Treg: regulatory T cell; MHC: major histocompatibility complex; Ag: antigen

*Source: Company data*

### *Advantage and Market Opportunity*

LAE005 was tested in a binding assay on either human or non-human primate cynomolgus monkey PD-L1-transfected 300.19 cells. In three replicate experiments, LAE005 bound to human PD-L1 cell line with a KD of 0.265 ± 0.048 nM and non-human primate PD-L1 cell line with a KD of 0.559 ± 0.101 nM (0.08 μg/ml). LAE005 was tested for its ability to block the binding of PD-1 and B7.1 to PD-L1 expressed on 300.19 cells. LAE005 blocked the PD-1 ligand with an $IC_{50}$ of 0.021 ± 0.145 nM (0.003 μg/ml) and the B7-1 ligand with an $IC_{50}$ of 0.104 ± 0.030nM (0.015 μg/ml).

We believe there is a significant commercial opportunity in China for PD-1/PD-L1 class of drugs. The global PD-1/PD-L1 market has grown rapidly in the past five years, from US$10.1 billion in 2017 to US$34.4 billion in 2021 at a CAGR of 35.9%. Currently available clinical data suggest that some of the most prevalent cancers globally and in China, such as lung, gastric, liver and esophageal cancers, are responsive to the PD-1/PD-L1 class of drugs. Taking into account of the other cancer types (such as bladder, melanoma and kidney cancers) that are also responsive to the PD-1/PD-L1 class, the overall annual incidence of cancers potentially responsive to the treatment of PD-1/PD-L1 antibodies in China was over four million in 2021.

Despite encouraging monotherapy clinical results, anti-PD-1/PD-L1 agents as monotherapy are not always effective. A large number of patients did not benefit from anti-PD-1/PD-L1 therapy (primary resistance). Some responders relapsed after a response period (acquired resistance). Some patients had to pause the ongoing treatment because of the development of immune-related adverse events. Therefore, combinatorial therapies targeting the PD-1/PD-L1 pathway and resistance mechanisms provide a rationale for sensitizing the resistant patients. Based on the limited therapeutic effect of anti-PD-1/PD-L1 as monotherapy, it is urgent to explore effective combinatorial approaches to overcome anti-PD-1/PD-L1 therapy's resistance and provide insights into clinical applications. Combined therapies of PD-1/PD-L1 blockade with adjunctive strategies have demonstrated its potential in improving the probability, duration, and potency of clinical activity. We are evaluating the therapeutic potential of combination therapy of LAE005 in combination with AKT inhibitor LAE002 for the treatment of TNBC to demonstrate its efficacy profile.

Currently, there are seven FDA-approved PD-1/L1 monoclonal antibodies. There are more than 30 drugs in clinical trials globally.

**FDA Approved PD-1/L1 Monoclonal Antibodies**

| Company | Generic Name | Brand Name | FDA Approval Month | FDA Approval Indications |
|---|---|---|---|---|
| Merck | Pembrolizumab | KEYTRUDA® | 2014.9 | Melanoma, NSCLC, HNSCC, cHL, PMBCL, Urothelial Carcinoma, Gastric Cancer, Esophageal Cancer, Cervical Cancer, HCC, MCC, RCC, MSI-H/dMMR Cancer, MSI-H/dMMR CRC, Endometrial Carcinoma, TMB-H Cancer, cSCC, TNBC |
| BMS | Nivolumab | OPDIVO® | 2014.12 | Unresectable or Metastatic Melanoma, NSCLC, Malignant Pleural Mesothelioma, Advanced RCC, cHL, HNSCC, Urothelial Carcinoma, MSI-H/dMMR CRC, HCC, Esophageal Cancer, Gastroesophageal Junction Cancer and Esophageal Adenocarcinoma |
| Regeneron/ Sanofi | Cemiplimab | LIBTAYO® | 2018.9 | NSCLC, BCC, Metastatic or Locally Advanced CSCC |
| GSK | Dostarlimab | JEMPERLI® | 2021.4 | dMMR Recurrent or Advanced Endometrial Cancer or Solid Tumors |

| Company | Generic Name | Brand Name | FDA Approval Month | FDA Approval Indications |
|---|---|---|---|---|
| Roche | Atezolizumab | TECENTRIQ® | 2016.5 | Urothelial Carcinoma, NSCLC, SCLC, HCC, Melanoma, Alveolar Soft Part Sarcoma (ASPS) |
| Merck/Pfizer | Avelumab | BAVENCIO® | 2017.3 | Metastatic Merkel Cell Carcinoma, Locally Advanced or Metastatic Urothelial Carcinoma, Advanced RCC |
| AstraZeneca | Durvalumab | IMFINZI® | 2017.5 | NSCLC, ES-SCLC, Advanced Biliary Tract Cancer |

*Note:* Information as of April 30, 2023.

*Source: FDA, Literature Review, Frost & Sullivan analysis*

In China, there are 10 PD-1 monoclonal antibodies and five PD-L1 monoclonal antibodies approved by the NMPA. There are more than 30 drugs in clinical trials in China.

**NMPA Approved PD-1 Monoclonal Antibodies**

| INN | Trade Name | Company | Approval Date | Indications | Price (RMB) | Dosage | Injection Methods | 2020 Revenue ($Million) | NRDL Status | Annual Cost after PAP or NRDL (Thousand RMB) |
|---|---|---|---|---|---|---|---|---|---|---|
| Nivolumab | Opdivo | BMS | Jun-2018 | NSCLC, squamous cell carcinoma of the head and neck, adenocarcinoma of the stomach or gastroesophageal junction, pleural mesothelioma, esophageal cancer, urothelial cancer | 100mg: 9,250RMB; 40mg: 4,587RMB | 3mg/kg every 2 weeks | Intravenous | 6,992.0 (Global) | NO | 108.2 |
| Pembrolizumab | Keytruda | MSD | Jul-2018 | Melanoma, NSCLC, esophageal squamous cell carcinoma, head and neck squamous cell carcinoma, colorectal cancer, liver cancer, TNBC | 100mg: 17,918RMB | 2mg/kg every 3 weeks | Intravenous | 14,380.0 (Global) | NO | 93.2 |
| Toripalimab | Tuoyi 拓益 | Junshi (君實生物) | Dec-2018 | Melanoma, nasopharyngeal carcinoma, urothelial carcinoma, esophageal cancer, NSCLC | 80mg: 906RMB | 3mg/kg every 2 weeks | Intravenous | 160.5 | Class B | 57.4 |
| Sintilimab | Daboshu 達伯舒 | Innovent (信達生物) | Dec-2018 | Classical Hodgkin lymphoma, NSCLC, HCC, esophageal cancer, gastric cancer, gastroessophageal cancer | 100mg: 1080RMB | 200mg every 3 weeks | Intravenous | 359.7 | Class B | 36.7 |
| Camrelizumab | Airuika 艾瑞卡 | Hengrui (江蘇恒瑞) | May-2019 | Classical Hodgkin lymphoma, HCC, NSCLC, Esophageal squamous cell carcinoma, NPC | 200mg: 2,928RMB | 200mg every 2 weeks | Intravenous | 480.0 | Class B | 76.1 |
| Tislelizumab | Baizean 百澤安 | Beigene (百濟神州) | Dec-2019 | Classical Hodgkin lymphoma, urothelial carcinoma, HCC, NSCLC, nasopharyngeal cancer, esophageal cancer, MSI-H/dMMR solid tumor, gastric or gastroesophageal junction (G/GEJ) cancer | 100mg: 1450RMB | 200mg every 3 weeks | Intravenous | 165.6 | Class B | 49.3 |
| Penpulimab | Annike 安尼可 | Chia Tai Tianqing (正大天晴)/ Akeso Biopharma (康方生物) | Aug-2021 | Recurrent or refractory classical Hodgkin's lymphoma, NSCLC | 100mg: 4875RMB | 200mg every 2 weeks | Intravenous | NA | NO | 19.5 |
| Zimberelimab | Yutuo 譽妥 | WuXi Biologics (藥明生物)/ GloriaBio (譽衡生物) | Aug-2021 | Recurrent or refractory classical Hodgkin's lymphoma | 120mg: 3300RMB | 240mg every 2 weeks | Intravenous | NA | NO | 171 |
| Serplulimab | 漢斯狀 | Henlins (復宏漢霖) | Mar-2022 | MSI-H solid tumors, NSCLC, SCLC | 100mg: 5588RMB | 3mg/kg every 2 weeks | Intravenous | NA | NO | 285 |
| Pucotenlimab | 普佑恒 | 樂普生物 | Jul-2022 | MSI-H/dMMRsolid tumors, advanced melanoma | NA | 200mg every 3 weeks | Intravenous | NA | NO | - |

*Note:* Information as of April 30, 2023.

*Source: NMPA, Company Annual Report, Frost & Sullivan analysis*

**NMPA Approved PD-L1 Monoclonal Antibodies**

| INN | Trade Name | Company | Approval Date | Indications | Price (RMB) | Dosage | Injection Methods | 2020 Revenue ($ Million) | NRDL Status | Annual Cost after PAP (Thousand RMB) |
|---|---|---|---|---|---|---|---|---|---|---|
| Atezolizumab | Tecentriq | Roche | Feb-2020 | SCLC, HCC | 1,200mg: 32,800RMB | 1200mg every 3 weeks | Intravenous | 2,965.0 (Global) | NO | 295.2 |
| Durvalumab | Imfinzi | AZ | Dec-2019 | NSCLC | 120mg: 6,066RMB; 500mg: 18,088RMB | 10mg/kg, every 2 weeks | Intravenous | 2,042.0 (Global) | NO | 217.1 |
| Envafolimab | 恩維達 | 3D Medicines/ Al Phamab Oncology/ Simcere | Nov-2021 | MSI-H/dMMR advanced solid tumor | 200mg: 5,980RMB | 400mg every 4 weeks | Subcutaneous | NA | NO | 71.8 |
| Sugemalimab | 擇捷美 | Cstone Pharma | Dec-2021 | NSCLC | 600mg: 12,375RMB | 1200mg every 3 weeks | Intravenous | NA | NO | 420 |
| Adebrelimab | 艾瑞利 | Hengrui (江蘇恒瑞) | Mar-2023 | SCLC | NA | NA | Intravenous | NA | NO | NA |

*Note:* Information as of April 30, 2023.

*Source: NMPA, Company Annual Report, Frost & Sullivan analysis*

### *Licenses, Rights and Obligations*

On February 4, 2020, we entered into a license agreement with Novartis. According to the license agreement, Novartis grants us an exclusive and sub-licensable license to practice Novartis's and its affiliates' interest in the licensed know-how and patents to research, develop and commercialize LAE005 worldwide. For more details, please see "– Collaboration and Licensing Arrangements – Collaboration with Novartis – LAE005 License Agreement" in this section.

### *Clinical Development Plan*

When we in-licensed LAE005 from Novartis, LAE005 has been evaluated by Novartis in several Phase I studies for safety and efficacy in cancer treatment. LAE005 was also in a Phase I study as a single agent and in combination with PDR001 (spartalizumab, an anti-PD-1 monoclonal antibody developed by Novartis) in adult patients with advanced malignancies. We have initiated a Phase I/II trial in China for the treatment of TNBC in combination with LAE002 and nab-paclitaxel to continue to leverage the clinical value and explore AKT's potential. We plan to obtain the Phase I read-out in the fourth quarter of 2023, initiate the Phase II study in China in the first quarter of 2024 and complete the Phase II study in China in the fourth quarter of 2025. This study is planned to be expanded to a MRCT trial in China and the U.S. at the registrational stage.

We had not received any relevant regulatory agency's concerns or objections to our clinical development plans as of the Latest Practicable Date, nor did any material unexpected or adverse changes had occurred since the date of issue of relevant regulatory approvals for LAE005.

## WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET LAE005 SUCCESSFULLY.

### LAE003: A Potentially Potent ATP Competitive AKT Inhibitor

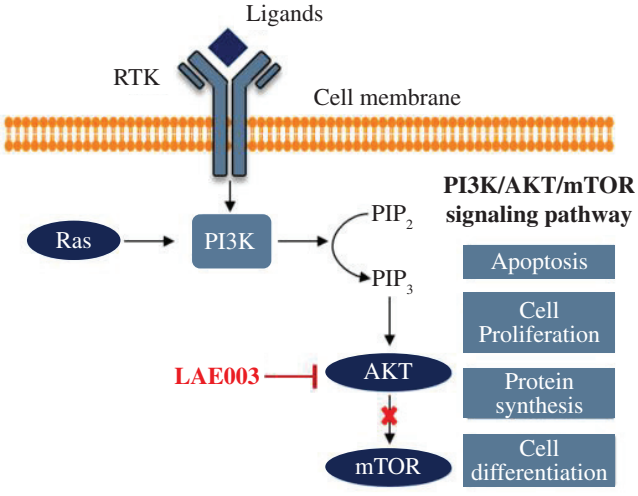
*Overview*

LAE003 is expected to be a potent ATP competitive AKT inhibitor. In the pre-clinical studies, LAE003 showed high potency and selectivity to AKT1, AKT2 and AKT3. LAE003 is currently at the clinical stage for cancer treatment and we are re-purposing it for the treatment of hereditary hemorrhagic telangiectasia and proteus syndrome. We expect LAE003 to be our lead drug candidate in the rare disease therapeutic area.

*Mechanism of Action*

AKT is a family of serine/threonine-specific protein kinase, which acts as a mediator in many biological processes like glucose metabolism, apoptosis, cell differentiation and transcription. Three members in the AKT family have been identified until now, namely AKT1, AKT2 and AKT3. While AKT2 is mostly involved in glucose transport and AKT3 is highly expressed in brain tissue, AKT1 plays a key role in cellular survival and metabolism mechanisms. LAE003 is a low nanomolar adenosine triphosphate competitive, AKT kinase inhibitor that inhibits baculovirus expressed, full-length human AKT1, 2 and 3 catalyzed phosphorylation of a synthetic peptide substrate.

The diagram below illustrates the mechanism of action of LAE003:




*Glossary & abbreviation:*

RTK: receptor tyrosine kinase; mTOR: mammalian target of rapamycin; PIP2: phosphatidylinositol(4,5)bisphosphate; PIP3: phosphatidylinositol-3,4,5-triphosphate

*Source: Company data*

***Advantage and Market Opportunity***

LAE003 is expected to be a high potent and selective AKT inhibitor. To characterize the potency and selectivity of LAE003, the ability of LAE003 to inhibit baculovirus expressed full-length human AKT 1, 2 and 3 catalyzed phosphorylation of a synthetic peptide substrate was examined. The results showed that LAE003 inhibited AKT 1, 2 and 3 with $IC_{50}$ values of 2, 16 and 4 nM, respectively, which approached the nominal concentrations of enzymes used (20 nM) in the kinase assays. Ki* values were further determined in a filter binding assay using lower enzyme concentrations (0.1, 0.7, and 0.2 nM for human AKT 1, 2 and 3, respectively). Ki* values were 0.1, 1.4, and 1.5 nM in this more sensitive assay format for AKT 1, 2 and 3, respectively. To confirm the Ki* value against AKT1, the potency and binding kinetics of LAE003 for AKT1 were determined in a continuous fluorescence intensity assay using Sox-peptide (Sox-AKT-tide) and progress curve analysis. The results showed that LAE003 inhibited AKT1 with a Ki* value of 0.066 nM.

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant inherited disorder of blood vessel formation characterized by mucocutaneous and visceral vascular malformations resulting in direct communication between arterioles and venules. This process is thought to occur stepwise, starting with dilation of postcapillary venules, followed by arteriolar dilation and then loss of the intervening capillary bed. Because of abnormal vascular development, patients with HHT tend to form large vascular networks between the veins and arteries, including telangiectasia, arteriovenous malformation (AVM) and arteriovenous fistula. Although there is no cure for HHT, there are treatments for the symptoms of HHT. The cause of HHT is loss of function mutations in ALK1/ENG/SMAD. Studies have demonstrated that ALK1/ENG/SMAD mutation causes activation of the PI3K/AKT and VEGFR2 pathway in endothelial cells. Recent studies have revealed that PI3K-AKT signaling is over-activated in several HHT models and that its inhibition reduces the AVMs. As an AKT inhibitor, we believe LAE003 can reduce the AVMs to relieve the symptoms of HHT.

Proteus syndrome is a rare complex syndrome involving clinical presentation with atypical skeletal growth. The onset may involve any site of the body and typically occurs during infancy. Therapy for this disorder is limited to supportive care and surgical intervention. Genetic mosaicism, such as activating AKT1 mutations, has been suggested to be an important causes of Proteus syndrome. As LAE003 can potently inhibit these AKT mutations, we believe LAE003 exhibits the potential to be an effective therapy for Proteus syndrome.

***Licenses, Rights and Obligations***

On May 9, 2018, we entered into a license agreement with Novartis. According to the license agreement, Novartis grants us an exclusive, royalty-bearing, sub-licensable and assignable license regarding the licensed patent and data to develop, use, manufacture or have manufactured and/or commercialize LAE003 in any and all therapeutic, prophylactic and/or diagnostic uses in humans worldwide. For more details, please see "– Collaboration and Licensing Arrangements – Collaboration with Novartis – LAE002 and LAE003 License Agreement" in this section.

*Clinical Development Plan*

When we in-licensed LAE003 from Novartis, LAE003 was in several Phase I, Phase II clinical trials for various cancer indications. We are re-purposing LAE003 for treating rare diseases such as hereditary hemorrhagic telangiectasia and Proteus syndrome. To further discover the therapeutic potential of our LAE003, we will continue to explore combination therapies that potentially may have better clinical outcomes than monotherapy. To that end, we are exploring potential opportunities to cooperate with global partners on the development of LAE003.

The differences between LAE002 and LAE003 include compound composition and inhibitory potency against AKT1, AKT2 and AKT3. In our commercial consideration to avoid LAE003 becoming a competitor to LAE002, based on their different compound composition and inhibitory potency against AKT, LAE002 is purposed for cancer treatment while LAE003 is repurposed for rare disease treatment. To avoid potential future competition, we plan to require the potential partners undertake not to engage, participate or assist in engaging or participating, directly or indirectly, in any development, manufacture and commercialization of LAE003 in the field of cancer therapy. Although LAE002 and LAE003 were licensed under the same license agreement, our post-licensing development and commercialization of LAE002 and LAE003 are independent.

**WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET LAE003 SUCCESSFULLY.**

**PRE-CLINICAL-STAGE DRUG CANDIDATES**

We have also developed a rich pipeline of pre-clinical drug candidates with strong pre-clinical validation and market potential. To leverage our knowledge in oncology and liver fibrosis and to build synergies between programs targeting both areas, we are focusing our research on immune cells important for cancer immune surveillance and liver fibrosis reversal. We are developing multiple monoclonal and bispecific antibodies against key regulatory pathways of NK cells and T cells, and bi-functional NK engagers targeting cancer cells and activated hepatic stellate cells (aHSC). They are in various stages of drug discovery, and we plan to have at least one molecule to enter the clinical stage each year on average, starting in 2023.

**Oncology Drug Candidates**

Although ICIs have been approved for a wide array of cancer indications worldwide, a large number of patients with solid tumors are not responsive to ICIs treatments or develop drug resistance ultimately. We are developing immuno-oncology agents that target the mechanisms for ICI-resistance. We are particularly interested in the inhibitory receptors expressed by cancer infiltrating lymphocytes (i.e., LAE102, LAE109, LAE111, LAE113 and LAE117) and ligands/receptors expressed on or produced by the cancer cells (i.e., LAE112). We believe that these inhibitory pathways represent targets for developing anticancer agents that could reverse resistance to ICIs.

Our most advanced internally developed candidate is the activin receptor ActRIIA mAb, LAE102. As a member of the TGFβ family, activin is attracting an increasing interest due to its multifunctional role in cancer development, particularly its immunomodulatory function. In several cancer types, high expression of activin is associated with shorter survival. LAE102 is a potentially potent and selective ActRIIA mAb that has demonstrated anti-tumor activity in pre-clinical animal models. Furthermore, it increased the bodyweight of cancer-bearing animals. We obtained the IND approval of LAE102 in May 2023, and plan to initiate the Phase I trial in the U.S. in the first half of 2024.

**Liver Fibrosis Drug Candidates**

In addition to our pre-clinical-stage oncology drug candidates, we are also developing a series of pre-clinical drug candidates for liver fibrosis which represents another therapeutic area with huge unmet medical needs. We have designed and validated a TGFβ inhibitor, LAE106, active only in fibrotic tissues. Liver fibrosis is the excessive accumulation of extracellular matrix proteins including collagen that occurs in chronic liver diseases. According to Frost & Sullivan, the global and China prevalence of liver fibrosis is expected to increase from 804.5 million and 139.3 million in 2021 to 966.5 million and 152.3 million in 2030, respectively. Control or cure of viral infection by patients after the removal or elimination of causative agent has shown that liver fibrosis is reversible, and recent evidence suggests that it can be reversed by regulating the immune system. Currently, there is no effective anti-liver fibrosis drug approved globally. Thus, there is unmet medical need for anti-fibrotic therapies to prevent liver disease progression.

**WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET OUR PRE-CLINICAL-STAGE DRUGS SUCCESSFULLY.**

**COLLABORATION AND LICENSING ARRANGEMENTS**

**Collaboration with Novartis**

***LAE001 License Agreement***

On June 30, 2017, we entered into a license agreement ("**LAE001 License Agreement**") with Novartis, a subsidiary of Novartis AG (NYSE: NVS), a multinational group of companies specializing in the research, development, manufacturing and marketing of healthcare products led by innovative pharmaceuticals and also including high-quality generic pharmaceuticals. Its major therapeutic focus includes cancer, cardiovascular, renal & metabolism diseases, immunology & dermatology, ophthalmology, neuroscience, and respiratory diseases. Its principal place of business locates in Basel, Switzerland. Novartis is one of our shareholders.

Novartis is the sole and exclusive owner of the intellectual property rights of LAE001. According to the LAE001 License Agreement, Novartis grants to us an exclusive, royalty-bearing, sub-licensable and assignable license regarding the licensed patents and data to develop, use, manufacture or have manufactured and/or commercialize LAE001 in any and all therapeutic, prophylactic and/or diagnostic uses in humans ("**LAE001 Field**") worldwide. Novartis grants to us a non-exclusive, sublicensable, assignable license regarding

themanufacturing technology to manufacture or have manufactured the LAE001 for development or commercialization of LAE001 in the LAE001 Field worldwide. The non-exclusive license of manufacturing technology of LAE001 granted by Novartis is in line with market practice and Novartis utilizes the same manufacturing technology for many of the products it manufactures. No other company has the legal right to manufacture LAE001 as we have the sole and exclusive manufacturing rights to the compounds of LAE001.

Novartis shall transfer to us all the data and information related to LAE001 and/or drug product manufactured therefrom for use in the LAE001 Field worldwide owned or controlled by Novartis or its affiliates and available in the global databases and archives, including relevant know-how related to the manufacturing of the LAE001 and/or drug products manufactured therefrom. As of the Latest Practicable Date, all such information, including know-how, had been transferred to us. We will be the sole owner of any inventions, know-how or similar IP rights conceived, created, reduced to practice or/and developed by us arising from our activities under the agreement.

In consideration of the licenses and rights granted to us, the upfront payment and the maximum milestone payments payable by us amount to US$33.5 million in the aggregate, which includes US$1.0 million non-refundable upfront payment and US$32.5 million milestone payments, consisting of development milestone payments divided into individual payments between US$5.0 million to US$10.0 million upon (a) receipt of regulatory approval for two different indications in China, (b) receipt of regulatory approval for the use in the LAE001 Field in the U.S, (c) receipt of regulatory approval for the use in the LAE001 Field in one or more major EU markets, and (d) receipt of regulatory approval in Japan. We are also obligated to pay tiered royalties ranging from a single-digit percentage to a low teen percentage of annual net sales of LAE001. As of December 31, 2022, we have paid US$1.0 million under the LAE001 License Agreement.

Unless terminated earlier, the LAE001 License Agreement shall continue in full force and effect in perpetuity. Novartis and we may terminate the LAE001 License Agreement upon a written mutual agreement. All rights and licenses granted to us under the LAE001 License Agreement will immediately terminate upon termination by either party. Novartis has the right to terminate the agreement by serving written notice on us only upon the occurrence of events including (i) we fail to pay the undisputed amount of upfront, milestone and royalty fees, and we fail to remedy such failure within 30 days of receipt of a written notice from Novartis specifying such failure; (ii) we fail to comply or are incompliant with the 2017 Shareholders Agreement, according to which, (a) we should issue 3,288 shares to Novartis AG so that Novartis AG can indirectly hold 5% equity interest in Laekna Therapeutics upon closing of the LAE001 License Agreement and (b) Novartis AG's ultimate beneficial interest in Laekna Therapeutics shall be maintained at 5% until the valuation of Laekna Therapeutics reaches US$70 million, above which, Novartis AG's ultimate beneficial interest in Laekna Therapeutics shall be diluted on a pro rata basis. The valuation of Laekna Therapeutics was determined at each round of [**REDACTED**] Investment, taking into account its business prospects and the research and development of our drug candidates at the time of investment; (iii) we change our organizational structure without Novartis' prior written consent in a way

that our Company, Laekna HK and Laekna Therapeutics are no longer affiliates; (iv) occurrence of an "Insolvency Event", which means, in relation to a party (Novartis or our Company), any occurrence of the following: (a) a party is the subject of voluntary or involuntary bankruptcy proceedings instituted on behalf of or against Laekna, Inc., except for involuntary bankruptcy proceedings which are dismissed within 120 days, (b) an administrative receiver, receiver and manager, interim receiver, custodian, sequestrator or similar officer is appointed for substantially all of the assets of a party, (c) a resolution to wind up our Company shall have been passed other than a resolution of the solvent reconstruction or reorganization of a party, or (d) a resolution passed by a party's board of directors to make an application for an administration order or to appoint an administrator for substantially all of the assets of such party; or (v) it has been adjudicated by a court with competent jurisdiction that we have materially breached our obligation to use commercially reasonable efforts to develop, manufacture and commercialize LAE001 in the LAE001 Field worldwide and fails to cure such breach within a period of 60 days after such court adjudication. We also have the right to terminate the license agreement by serving written notice on Novartis only upon the occurrence of the events including (a) Novartis has materially breached its obligation under the LAE001 License Agreement and fail to cure such breach, (b) an Insolvency Event occurred, and (c) upon 45 days' written notice for material scientific, technical or medical reasons. We granted 776,437 ordinary shares to Novartis AG and Novartis to fulfill our obligations under the 2017 Shareholders Agreement, including (i) the issuance of 3,288 shares to Novartis AG in July 2017 to fulfill the share subscription obligation after signing the LAE001 License Agreement, and on April 4, 2018, Novartis AG transferred all its beneficial interest in Laekna Therapeutics to Novartis, (ii) the issuance of 563,315 shares to Novartis in April 2018 to fulfill the anti-dilution obligation resulting from the dilution due to Series Seed financing of our Company, and (iii) the issuance of 209,834 shares to Novartis in May 2018 to fulfill the anti-dilution obligation resulting from the dilution due to Series A financing of our Company. The 2017 Shareholders Agreement had been superseded by the 2018 Shareholders Agreement.

Under the LAE001 License Agreement, we will use commercially reasonable efforts to develop, manufacture and commercialize LAE001 at our own costs and expenses and conduct the development activities. According to the LAE001 License Agreement, our commercially reasonable efforts with respect to the development of LAE001 include (i) development activities in relation to prostate cancer, and (ii) that we may pursue another indication besides prostate cancer such as estrogen dependent endometrial cancer. Under the LAE001 License Agreement, we shall provide Novartis with written summary report periodically summarizing our R&D activities performed and anticipated R&D plans.

Our Directors are of the view that we have been using commercially reasonable efforts in the development of LAE001 and the associated risk of the LAE001 License Agreement with Novartis being terminated is low, on the following basis: (i) we have completed a Phase I clinical trial of a Phase I/II study of LAE001 for mCRPC and initiated the Phase II clinical trial, which is in line with the R&D plan required under the LAE001 License Agreement. For more details on the post-licensing R&D activities of LAE001, please see "– Clinical Stage Candidates – Core Product LAE001: A dual CYP17A1/CYP11B2 inhibitor – Post-licensing R&D activities". Actual R&D expenses attributable to LAE001 during the Track Record Period

were RMB54.1 million; (ii) our plans for registration and commercialization of LAE001 have been approved by Novartis; (iii) we expect to continue our commercially reasonable efforts in the development and commercialization of LAE001. For example, we plan to continue our development and commercialization of LAE005 and LAE002, and they are intended to be used for LAE001 as combination therapies, respectively, among other applications. For more details on the development plan of LAE001, see "– Clinical Stage Candidates – Core Product LAE001: A dual CYP17A1/CYP11B2 inhibitor – Clinical Development Plan"; (iv) we plan to use a portion of the net [**REDACTED**] from the [**REDACTED**] for the development and commercialization of LAE001. See "Future Plans and Use of [**REDACTED**]" in this document for further details; and (v) during the Track Record Period and up to the Latest Practicable Date, we provided Novartis with written summary report periodically summarizing our R&D activities performed and anticipated R&D plans for LAE001, and Novartis had not raised any concerns on our clinical progress or questioned on the commercially reasonableness of our efforts.

As of the Latest Practicable Date, we had no intention or plan to out-license LAE001 in the domestic or overseas markets.

***LAE002 and LAE003 License Agreement***

On May 9, 2018, we entered into a license agreement ("**LAE002 and LAE003 License Agreement**") with Novartis. Novartis is the sole and exclusive owner of the intellectual property rights of LAE002 and LAE003. The rights and details of LAE002 under the LAE002 and LAE003 License Agreement are the same as those of LAE003. According to the LAE002 and LAE003 License Agreement, Novartis grants to us a royalty-bearing, sub-licensable and assignable exclusive license to develop, use, manufacture or have manufactured and/or commercialize LAE002 and LAE003 in any and all therapeutic, prophylactic and/or diagnostic uses in humans (the "**LAE002 and LAE003 Field**") worldwide. Novartis grants to us a non-exclusive, sublicensable, assignable license regarding the manufacturing technology to manufacture or have manufactured the LAE002 and LAE003 for development or commercialization of LAE002 and LAE003 in the LAE002 and LAE003 Field worldwide. The non-exclusive license of manufacturing technology of LAE002 and LAE003 granted by Novartis is in line with market practice and Novartis utilizes the same manufacturing technology for many of the products it manufactures. No other company has the legal right to manufacture LAE002 and LAE003 as we have the sole and exclusive manufacturing rights to the compounds of LAE002 and LAE003.

Novartis shall transfer to us all the data and information related to LAE002 and LAE003 and/or drug product manufactured therefrom for use in the LAE002 and LAE003 Field worldwide owned or controlled by Novartis or its affiliates and available in the global databases and archives, including relevant IP and know-how related to the manufacturing of LAE002 and LAE003. As of the Latest Practicable Date, all such information, including know-how, had been transferred to us. We will be the sole owner of any improvements to the licensed patents and data and IP rights that are discovered, generated, developed, invented or created solely by us, our affiliates or third parties acting on us or our behalf while conducting

activities in connection with the development, manufacture and/or commercialization of LAE002 and LAE003, and will retain all of its rights, title and interest. We will use commercially reasonable efforts to develop, manufacture and commercialize LAE002 and LAE003 at our own costs and expenses and to conduct the development activities. "Commercially reasonable efforts" in the LAE002 and LAE003 license agreements has the same definition as in the LAE001 license agreement.

In consideration of the licenses under the agreement granted to us, we are required to pay the non-refundable upfront payment of US$5.0 million, US$242.5 million in milestone payments, consisting of (i) development milestone payments of up to US$57.5 million divided into individual payments between US$2.5 million to US$10.0 million upon either LAE002 or LAE003 (a) dosing of the first patient in the first visit in the first Phase III registrational clinical trial, (b) the first NDA acceptance; (c) receipt of regulatory approval for three different indications in China, (d) receipt of regulatory approval for three different indications in the U.S., (e) receipt of regulatory approval for three different indications in one or more EU markets; and (ii) sales milestone payments of up to US$185.0 million divided into individual payments upon achieving four different sales targets. Each milestone shall be deemed earned as of the first achievement of the respective milestone event and is payable one-time only. We are also obligated to pay tiered royalties ranging from a single-digit percentage to a low teen percentage of total annual net sales of LAE002 and LAE003. As of December 31, 2022, we have paid US$5.0 million under the LAE002 and LAE003 License Agreement.

Unless terminated earlier, the LAE002 and LAE003 License Agreement shall continue in full force and effect in perpetuity. Novartis and we may terminate the LAE002 and LAE003 License Agreement upon a written mutual agreement. All rights and licenses granted to us under the LAE002 and LAE003 License Agreement will immediately terminate upon termination by either party. Novartis has the right to terminate the agreement by serving written notice on us only upon the occurrence of events including (i) we fail to pay the undisputed amount of upfront, milestone and royalty fees, and we fail to remedy such failure within 30 days of receipt of a written notice from Novartis specifying such failure; (ii) we fail to comply or are incompliant with the 2018 Shareholders Agreement, according to which, (a) we should issue 165,200 shares to Novartis so that Novartis can hold 6% equity interest in Laekna Therapeutics upon closing of the LAE002 and LAE003 License Agreement and (b) Novartis' ultimate beneficial interest in Laekna Therapeutics shall be maintained at 6% until the valuation of Laekna Therapeutics reaches US$70 million, above which, Novartis' ultimate beneficial interest in Laekna Therapeutics shall be diluted on a pro rata basis. The valuation of Laekna Therapeutics was determined at each round of [**REDACTED**] Investment, taking into account its business prospects and the research and development of our drug candidates at the time of investment; (iii) we change our organizational structure without Novartis' prior written consent in a way that our Company, Laekna HK and Laekna Therapeutics are no longer affiliates; (iv) Insolvency Events, which has the same definition as in the LAE001 license agreement; or (v) it has been adjudicated by a court with competent jurisdiction that we have materially breached our obligation to use commercially reasonable efforts to develop, manufacture and commercialize LAE002 and LAE003 in the LAE002 and LAE003 Field worldwide and fails to cure such breach within a period of 60 days after such court

adjudication. We also have the right to terminate the license agreement by serving written notice on Novartis only upon the occurrence of the events including (i) Novartis has materially breached its obligation under this agreement, (ii) Insolvency Events occurred, and (iii) upon 45 days' written notice for material scientific, technical or medical reasons. We granted 165,200 ordinary shares after signing the LAE002 and LAE003 License Agreement in May 2018 to Novartis to fulfill the anti-dilution obligation under the 2018 Shareholders Agreement. Since the date of the Series B financing, Laekna Therapeutics has been valued at over US$70 million. We are not obligated to issue additional shares to Novartis in the future to maintain the agreed equity interest percentage should the valuation of Laekna Therapeutics subsequently fall below US$70 million as the 2017 Shareholders Agreement had been superseded by the 2018 Shareholders Agreement, which had then been superseded by the Series D Shareholders Agreement. The Series D Shareholders Agreement does not contain such anti-dilution mechanism.

Under the LAE002 and LAE003 License Agreement, our commercially reasonable efforts with respect to the development of LAE002 include (i) we will build on Novartis' Phase I/II LAE002 study "an open-label Phase I/II study of LAE002 in combination with carboplatin and paclitaxel in subjects with PROC", advance LAE002 to a global Phase III registrational trial study, initially focusing on market approval in the U.S., EU and China; (ii) we will conduct pre-clinical and clinical trials to evaluate if LAE002 alone or combine with LAE001 and prednisone have benefits in mCRPC patients relapsed after abiraterone or enzalutamide; (iii) we will conduct both pre-clinical and clinical study to evaluate whether LAE002 and LAE001 combining with endocrine therapies will be effective to treat the relapsed breast cancer carrying PTEN mutation by controlling both ER/PR and AKT activities; (iv) we will seek a partner to combine immune-oncology therapy for expanding the indications of LAE002; (v) we will explore other oncology indications such as gastric cancer, TNBC, liver cancer and esophageal cancer carrying PTEN mutation. If a proof-of-concept is achieved, we will initiate registration studies for NDA approval. Our commercially reasonable efforts with respect to the manufacturing of LAE002 allow us to initially work with CMOs on the manufacturing of LAE002 and LAE003 for clinical uses. In the long term, we may consider to transfer the manufacture technology to a CMO in China based on quality and economics considerations.

To demonstrate our "commercially reasonable efforts", we shall provide Novartis with a written summary report periodically summarizing our R&D activities performed and anticipated R&D plans.

Our Directors are of the view that we have been using commercially reasonable efforts in the development of LAE002 and the associated risk of the LAE002 and LAE003 License Agreement with Novartis being terminated is low, on the following basis: (i) our current clinical studies for LAE002 are in line with the R&D plans required by Novartis. For more details on the post-licensing R&D activities of LAE002, please see "– Clinical Stage Candidates – Core Product LAE002: An ATP competitive AKT inhibitor – Post-licensing R&D activities". Actual R&D expenses attributable to LAE002 during the Track Record Period were RMB271.7 million; (ii) our registration and commercialization plans for LAE002 have been approved by Novartis; (iii) we expect to continue our commercially reasonable efforts in the development and commercialization of LAE002. For example, we plan to continue our

development and commercialization of LAE005 and LAE001, and they are intended to be used for the LAE002 as combination therapies, respectively, among other applications. For more details on the development plan of LAE002, see "– Core Product LAE002: An ATP competitive AKT inhibitor – Clinical Development Plan"; (iv) we plan to use a portion of the net [**REDACTED**] from the [**REDACTED**] for the development and commercialization of LAE002. See "Future Plans and Use of [**REDACTED**]" in this document for further details; and (v) during the Track Record Period and up to the Latest Practicable Date, we provided Novartis with written summary report periodically summarizing our R&D activities performed and anticipated R&D plans for LAE002, and Novartis had not raised any concerns on our clinical progress or questioned on the commercially reasonableness of our efforts.

As of the Latest Practicable Date, we had no intention or plan to out-license LAE002 in the domestic or overseas markets.

***LAE005 License Agreement***

On February 4, 2020, we entered into a license agreement ("**LAE005 License Agreement**") with Novartis. According to the LAE005 License Agreement, Novartis grants to us an exclusive and sub-licensable license to practice Novartis' and its affiliates' interest in the licensed know-how and patents to research, develop and commercialize LAE005 worldwide. The manufacturing technology of LAE005 is not licensed to us and we can use our own manufacturing process for LAE005. As the manufacturing of LAE005 is not exclusively dependent on Novartis' manufacturing technology and Novartis has transferred the analytical manufacturing method to us, we cooperated with CDMOs on the manufacturing of LAE005 during the Track Record Period. As of the Latest Practicable Date, we had not experienced any obstacles in the manufacturing of LAE005. We may sublicense (through multiple tiers) the license at any time at our sole discretion to our affiliates, CROs, CDMOs, local and regional distributors, or other similar fee-for-service providers without notice to Novartis. As of the Latest Practicable Date, we had no sublicensing plan for LAE005.

Novartis is the sole and exclusive owner of the intellectual property rights of LAE005, save as one patent family that is jointly owned by President & Fellow of Harvard College, Dana Farber Cancer Inst. Inc. and Novartis AG. For details, see "– Intellectual Property" below in this section. President & Fellow of Harvard College and Dana Farber Cancer Inst. Inc. agreed for Novartis to license their jointly owned patent of LAE005 to us. Novartis shall transfer to us all the data and information relating to the LAE005. As of the Latest Practicable Date, all such information, including know-how, had been transferred to us. All know-how and patent rights that are created, conceived of, or reduced to practice by or on behalf of us, our affiliates or our agents and the practice of the licenses granted thereafter will be owned by us.

Novartis should continue funding and managing a LAE005 related clinical study identified as a study of LAE005 single agent and in combination with PDR001 (spartalizumab, an anti-PD-1 monoclonal antibody developed by Novartis) in patients with advanced malignancies (NCT02936102) ("**Ongoing Clinical Trial**") until they are completed in the ordinary course of Novartis' operations. No IND or clinical trial applications ("**CTA**") will be transferred to us. Nevertheless, we have the right to use the data and information in all Ongoing

Clinical Trial related regulatory filings, and establish and file all necessary documentation with regulatory authorities to support our own IND or CTA and further development of the LAE005. Other than for the Ongoing Clinical Trial, we will be solely responsible for all regulatory matters relating to the development of the LAE005 at our own costs and expenses. By ourselves or through our affiliates or sublicensees, we will use commercially reasonable efforts to develop the LAE005 and obtain regulatory approvals in at least one of the following markets, the U.S., one of the major EU countries, either Japan or China. "Commercially reasonable efforts" in the LAE005 license agreements has the same definition as in the LAE001 license agreement.

In consideration of the licenses and rights granted to us, the upfront payment and the maximum milestone payments payable by us amount to US$128.0 million in the aggregate, which consist of US$10.0 million in non-refundable upfront payment, and US$118.0 million in milestone payments, consisting of (i) development milestone payments of up to US$28.0 million divided into individual payments between US$2.0 million to US$10.0 million upon (a) the first visit of the first patient to the first registrational trial, (b) acceptance of a biologic license application in any jurisdiction or application for the authorization to market the product in any country or group of countries outside the U.S., (c) regulatory approval for three different indications; and (ii) sales milestone payments of up to US$90.0 million divided into individual payments upon achieving three different sales targets. We are also obligated to pay tiered royalties calculated ranging from a single-digit percentage to a low teen percentage of annual net sales of LAE005. As of December 31, 2022, we have paid US$10.0 million under the LAE005 License Agreement.

Suppose either Novartis or us is in material breach of any material obligation, the non-breaching party may give written notice to the breaching party specifying the claimed particulars of such breach, and in the event, such material breach is not cured within 90 days after such notice, the non-breaching party will have the right to terminate the agreement immediately by giving written notice to the breaching party to such effect. If any Insolvency Events occurs, which has the same definition as in the LAE001 license agreement, we will give immediate notice to Novartis of such occurrence, and Novartis will have the right to terminate this agreement by written notice immediately. We may also terminate the agreement without cause at any time on 90 days' prior written notice. All rights and licenses granted to us under the LAE005 License Agreement will immediately terminate upon termination by either party.

After we in-licensed LAE005, we designed a clinical trial to explore the therapeutic potential of the combination therapy of LAE002 and LAE005 in patients with TNBC. We conducted post-licensing R&D activities, including (i) preparing the clinical trial design/framework and protocol; (ii) coordinating with the FDA for the review and approval of our clinical trial, (iii) coordinating all post-licensing clinical development activities, (iv) designing and coordinating the selection process for qualified CROs to assist in engaging clinical sites and coordinating clinical studies once commenced; and (v) supervising the clinical studies. Actual R&D expenses attributable to LAE005 during the Track Record Period were RMB32.0 million. We plan to use a portion of the net [**REDACTED**] from the [**REDACTED**] for the R&D of LAE005. See "Future Plans and Use of [**REDACTED**]" in this document for further details.

**Collaboration with Innovent**

On July 6, 2021, we entered into a collaboration agreement ("**Innovent Collaboration Agreement**") with Innovent Biologics (Suzhou) Co. Ltd. ("**Innovent**"), a subsidiary of Innovent Biologics, Inc. (HK: 1801), a Hong Kong-listed Chinese biopharmaceutical company. Innovent is an Independent Third Party to us.

According to the Innovent Collaboration Agreement, Innovent and we will collaborate in a clinical combination trial to evaluate the safety, pharmacokinetics, pharmacodynamics and preliminary efficacy of the concomitant and sequenced administration of LAE002 and sintilimab injection in subjects with solid tumors ("**Study**"). Innovent will supply the sintilimab injection for free for our use in the combination therapy study. Innovent will remain as the sole owner of all know-how and patents of sintilimab injection controlled by Innovent that are necessary for sintilimab injection's development. All know-how that is created, conceived or reduced to practice by us or Innovent, in the performance of the development activities under the Innovent Collaboration Agreement, and all patent rights claiming such know-how (other than these that solely relates to sintilimab injection or LAE002), shall be jointly owned by us and Innovent.

According to Frost & Sullivan, sintilimab is a marketed anti-PD-1 monoclonal antibody in China, and Innovent plans to commercialize sintilimab in the U.S. as well. It has been approved for seven indications, of which six have been included in the National Reimbursement Drug List (NRDL), including: (i) the treatment of relapsed or refractory classic Hodgkin's lymphoma after systemic chemotherapy; (ii) in combination with pemetrexed and platinum chemotherapy as the first-line treatment of non-squamous non-small cell lung cancer lacking EGFR or ALK driver mutations; (iii) in combination with gemcitabine and platinum chemotherapy as the first-line treatment of squamous non-small cell lung cancer; (iv) in combination with Byvasda (bevacizumab biosimilar injection) as the first-line treatment of unresectable or advanced hepatocellular carcinoma; (v) in combination with cisplatin plus paclitaxel or cisplatin plus 5-fluorouracil as the first-line treatment of esophageal squamous cell carcinoma; and (vi) in combination with chemotherapy as the first-line treatment of unresectable, locally advanced, recurrent or metastatic gastric or gastroesophageal junction adenocarcinoma. The seventh indication that has been approved but not yet included in the NRDL is the second-line treatment of EGFR mutated NSCLC patients that have failed EGFR-TKI therapies in combination with bevacizumab biosimilar and chemotherapy. As of the Latest Practicable Date, sintilimab had met their primary endpoints in a Phase II study as a second-line treatment of esophageal squamous cell carcinoma and another Phase III study as a second-line treatment for squamous NSCLC with disease progression following platinum-based chemotherapy. Sintilimab plus platinum-based chemotherapy conferred better anti-tumor efficacy and clinical benefits compared to chemotherapy alone, which led to FDA's acceptance for review of biological license application of sintilimab in the U.S. However, in March 2022, the FDA issued a complete response letter (CRL) indicating it cannot approve the biologics license application for sintilimab in combination with pemetrexed and platinum chemotherapy for the first-line treatment of advanced NSCLC. The FDA had concluded that the supporting data from the Phase III clinical trial, which had been conducted entirely in China, could not be applied to U.S. population. They noted that the study population was younger,

predominantlymale, and included higher rates of smokers than are generally found in the U.S. The CRL also included a recommendation for an additional clinical study, specifically a multiregional clinical trial comparing the first line standard of care therapy for metastatic NSCLC to sintilimab with chemotherapy utilizing a non-inferiority design with an overall survival as the endpoint. As of the Latest Practicable Date, sintilimab was not an approved product in the U.S.

We believe that the CRL issued by the FDA for sintilimab for the first-line treatment of advanced NSCLC will not have a material impact on the Study, on the basis that: (i) the combination study will be conducted in China and as of the Latest Practicable Date, we did not have any plan to conduct a combination study of LAE002 and sintilimab overseas in collaboration with Innovent; alternatively, even if we decide to develop the combination use of LAE002 and sintilimab outside of China in the future, the related Phase II or Phase III clinical trial may be modified or designed as a MRCT in order to include adequate enrollment in the U.S. to mitigate the concerns expressed in the CRL; (ii) despite the CRL, sintilimab may still be approved by the FDA in the future if the issues in the CRL were addressed; and (iii) the CRL is issued in relation to sintilimab as a first-line treatment for advanced NSCLC without prior PD-1/PD-L1 treatment, which is different from the indication for the Study (PD-1/PD-L1 resistant solid tumors), meaning that the CRL does not have a direct implication on the Study. As such, the CRL issued by the FDA for sintilimab for the first-line treatment of advanced NSCLC will not impact our clinical trial of LAE002 and sintilimab for the treatment of PD-1/PD-L1 resistant solid tumors.

We will be the sponsor of the Study and be responsible for obtaining all necessary approvals and clearances, including regulatory and institutional review board (IRB) approvals and customs clearances, for the conduct of the Study, including filing the IND to the NMPA. Innovent will reasonably cooperate with us to provide us any information for the sintilimab injection that is reasonably necessary to allow us to fulfill our obligations as the sponsor of the Study. We would conduct the Study and lead the development activities and shall use or retain personnel with sufficient skills and experiences as are required to accomplish efficiently and expeditiously the Study in a good scientific manner. We have the decision-making authority and are solely responsible for the daily operational activities.

Each party shall be solely responsible for its internal costs and expenses in connection with its conduct or support of any development activities. We shall be fully responsible for all the costs and expenses in connection with the conduct of the development activities for the Study and other activities required for the Study except for the cost of sintilimab injection, which Innovent shall provide for free.

Each party agrees that we and Innovent shall jointly own all joint collaboration technology. Each party has the right to use and exploit such joint collaboration technology both within and outside the scope of the Study, without the consent of the other party and without any accounting to the other party. For those countries where a specific license is required for a joint owner of a joint collaboration technology to exploit such joint collaboration technology in such countries, each party grants to the other party a perpetual, irrevocable, non-exclusive, worldwide, royalty-free, fully paid-up, transferrable and sub-licensable license, under such

party's right, title and interest in and to all joint collaboration technology to exploit such joint collaboration technology. As between the parties, title to all collaboration technology that solely relates to LAE002 shall be owned by us, and title to all collaboration technology that solely relates to the sintilimab injection shall be owned by Innovent.

Our collaboration is non-exclusive other than that, during the term of the Innovent Collaboration Agreement, (i) we, including through our affiliates, shall not collaborate with any third-party to conduct any clinical trial of combination therapy of LAE002 and any anti-PD-1 antibody in mainland China and (ii) Innovent, including through its affiliates, shall not collaborate with any third party to conduct clinical trial of combination therapy of sintilimab injection and any AKT inhibitor in mainland China.

## OUR PLATFORM

We believe that fully-integrated in-house R&D capabilities are critical to our success. We have built a biopharmaceutical platform to identify drug candidates against evidence-based and novel targets, increasing the efficiency and likelihood of success while reducing the cost of development. Our platform facilitates collaboration among different functional groups and feeds into early discovery and research to cultivate targets with clinical and commercial potential. Our platform integrates all the necessary capabilities to streamline our target-to-market timeline. Our platform spans research and development, CMC, quality assurance and control, regulatory affairs to commercialization.

### Research and Development

We believe research and development are critical to our future growth and our ability to remain competitive in the global biopharmaceutical market. Leveraging our global reach, we have been able to stay at the forefront of global biology and pharmaceutical research, source attractive business development opportunities, execute and closely monitor complex MRCTs. In the foreseeable future, with global rights attached to all our product candidates, we aim to penetrate both the China and overseas market and reap the geographically diversified economic rewards.

We are dedicated to enhancing our pipeline by leveraging our strong in-house R&D capabilities, from early stage drug discovery to clinical development. As of the Latest Practicable Date, our R&D team consisted of 58 employees. We also work with CROs to support our pre-clinical and clinical studies in China and other regions. Our R&D team members have extensive pre-clinical and clinical development experience, focusing on oncology and liver diseases. In 2021 and 2022, our R&D expenses were RMB173.3 million and RMB313.4 million, respectively.

Our R&D team is generally responsible for the global development of our Core Products and other pipeline products. For our internally discovered and developed drug candidates, we conducted clinical activities including: (i) coordinating all clinical development activities; (ii) designing the key aspects of the clinical study; (iii) designing and coordinating the selection

process for qualified CROs to assist in engaging clinical sites and coordinating clinical studies once commenced; (iv) supervising the clinical studies; and (v) overseeing extensive regulatory outreach and coordination in China and the U.S. For our in-licensed Core Products, we are responsible for developing the candidates in our licensed territories. We promptly commenced research and development activities after in-licensing drug candidates from our licensing partners. We have devoted a considerable amount of time and resources to the R&D of in-licensed drug candidates, and such efforts include but are not limited to: (i) the design of the clinical trials to be implemented in our licensed territories and proactive communication with relevant regulatory authorities to obtain the approvals; (ii) the preparation of clinical trials, including the selection of clinical CROs and clinical sites; and (iii) the manufacturing of clinical samples through our cooperation with CDMOs. Our drug discovery and pre-clinical R&D, clinical development, CMC and regulatory affairs teams have been working on the development of Core Products during the post-licensing period.

***Drug Discovery and Pre-clinical Development***

Our drug discovery and pre-clinical development team is led by Dr. Justin Gu, who has over 20 years of experience in early-stage drug discovery. The primary goal of our discovery team is to identify new targets and novel drug candidates in the oncology and liver fibrosis disease areas; and the key activities span from target discovery, hit to lead generation, PCC selection, IND enabling studies to IND filing. In addition, our team also conducts pre-clinical translational research to support the clinical development of our drug candidates. To complement our internal capabilities, the team worked closely with the local CROs which have significantly increased the speed and efficiency of our internal discovery effort. Except for LAE002, LAE001, LAE005 and LAE003, all other product candidates have been discovered and developed by our R&D team. Our key R&D personnel remained employed during Track Record Period and up to the Latest Practicable Date.

As of the Latest Practicable Date, among our drug discovery and pre-clinical R&D team members, over 40% obtained a post-graduate degree with 50% of them holding a Ph.D. degree. Our R&D team has made contributions to dozens of discovery programs. For our self-developed pipeline products, during the drug discovery stage, our drug discovery and pre-clinical R&D team explores new chemical properties, structure-activity-relationship (SAR) analysis based on the biological understanding of the disease, and carries out synthesis and structure optimization of the target molecules for potential drug candidates. During the drug evaluation stage, our drug discovery and pre-clinical R&D team coordinates and accomplishes pre-clinical R&D activities to evaluate product candidates' pharmacology, pharmacokinetics and toxicology. With our R&D platform, we are able to conduct a full range of pre-clinical R&D activities including product activity screening, studies of cellular functions of product candidates, product biochemical studies, biomolecule detection and others. Below are some of the highlights of our drug discovery and pre-clinical development capacities:

- We conduct extensive bioinformatics data mining to identify target and mechanism of action for oncology and liver fibrosis diseases. We design and implement detailed biochemical, cellular, and animal studies to identify the signaling pathway of the

target and to validate its role in disease. We try to build synergies between oncology and liver fibrosis disease area by focusing on the regulatory pathways of the immune cells, and on targets that are selectively expressed on cancer cells or activated hepatic stellate cells.

- Leveraging our internal antibody discovery expertise platform and our cooperation with CROs, we conduct extensive screenings to identify novel, potent and selective mAbs against the selected targets. Then we build bispecific or bifunctional antibodies based on our deep knowledge in disease biology and experience in antibody engineering.

- We conduct extensive *in vitro* functional characterization of our molecules, e.g. their effect in regulating the immune cell function and immune cell-mediated killing of cancer cells and aHSC cells. For this purpose, we established a comprehensive aHSC-depletion platform that enabled us to quickly and comprehensively evaluate the effect of our molecules on aHSC *in vitro*.

- We perform extensive pre-clinical proof-of-mechanism studies in animal models to build PK/PD relationship and to evaluate the antitumor or anti-fibrosis efficiency of our drug candidates. For this purpose, we use a wide variety of different models based on the mechanism of action of our drug candidates. Xenograft models in immune deficient mice are typically used for evaluating anti-tumor drug candidates. Syngeneic models in immune competent mice are the common choice for characterizing immune oncology drug candidates. For antifibrosis drug candidates, we use chemical- or diet-induced fibrosis models.

- After a drug candidate shows the desired activities in the proof-of-mechanism animal models and meet all the other criteria for a pre-clinical candidate (PCC), we will then move the candidate into CMC and pre-IND tox studies. Large quantity of our drug candidates will be manufactured by our CMC team in collaboration with our CRO partners. PK and long-term toxicity studies will be conducted in animals before filing for IND.

***Clinical Development***

*Clinical Development Team*

Our clinical development team is led by Dr. Yong Yue, who has over 20 years of experience in cancer treatment, especially in liver cancers. The clinical development team covers most of the key functions that enable us to execute well, from clinical development strategy, clinical development planning, setting up quality assurance and control system, to clinical trial design, trial operations, safety monitoring, data management, data analysis and programming, clinical supply, procurement, etc.

*Clinical Trial Design and Implementation*

Our clinical development team is responsible for our trial design and execution and manages the procedures of our clinical trials with the assistance of CROs and SMOs. Our rapid trial advancements are driven by our (i) extensive clinical development experience, (ii) well-designed trial protocols, (iii) multi-center trial strategy in close collaboration with trial sites (i.e., hospitals) and corresponding principal investigators (PIs), and (iv) efficient and effective trial execution.

For the Core Products and other pipeline products, as the sponsor of our clinical trials, our clinical development team is responsible for initiating and funding the trials, formulating trial protocols, managing the trial implementation throughout the whole process and across multiple clinical sites following the trial protocols and GCP. Our clinical development team designs and formulates trial protocols and prepares investigators' brochures based on the differentiated profile and target patient population of our drug candidates and clinical practice in China and the U.S. to maximize our drug candidates' clinical potential and to accelerate the regulatory approval process. Trial protocols usually include background and basic information, trial objectives and purpose, trial design and implementation approach.

Our clinical development team is also responsible for the selection of trial sites. We select trial sites based on multiple factors. We have entered into a cooperative relationship with numerous trial sites (i.e., hospitals) and PIs to support our clinical trials at different stages. We believe that these institutions' size and geographic diversity provide us with a significant advantage in implementing large-scale clinical trials and enable us to conduct multiple clinical trials concurrently.

In 2021 and 2022, we cooperated with seven and seven leading PIs, respectively, to conduct the clinical trials of our drug candidates. To the best of our knowledge, none of them has any past or present relationships with our Group, our Directors, shareholders, senior management or any of their respective associates. As the sponsor of our clinical trials, we take primary responsibility for the design and execution of the entire trial. Our clinical trial team formulates trial protocols and selects and engages trial sites and PIs to conduct clinical trials. The PIs are primarily responsible for conducting site-level clinical research activities according to our trial protocols and in accordance with laws, regulations, and the GCP Guideline, a quality standard for the overall conduct of the clinical trial. The PIs regularly communicate with us on the trial progress and observations to evaluate the efficacy and safety of our drug candidates. Each trial has a leading PI with primary responsibility to ensure compliance with trial protocol and good clinical practice over the entire trial. Through the trial process and with the assistance of CROs or SMOs, we closely monitor the trial activities, perform site audits, conduct an ongoing risk assessment and safety evaluation, review protocol deviated cases, and review clinical data to protect the safety of subjects and ensure the integrity of trial results. We collect and analyze trial data after the last subject completes the last visit to prepare documentation for regulatory approvals of our drug candidates. The roles and responsibilities of the PIs in our clinical trials are in line with the common industry practices. In accordance with the laws and regulations, we enter into agreements with the hospitals that

the PIs belong to and settle the fees and expenses with those hospitals. To avoid any potential conflict of interests, we do not have any agreements with or make any payment to the PIs directly. We conduct our clinical trials in accordance with the relevant laws and regulations in China in line with the common industry practice.

The following table sets forth the background of leading PIs of our clinical trials during the Track Record Period:

| | **Background** |
|---|---|
| PI A | He is a director of the Multi-disciplinary Team for GU cancer and president of the Chinese Anti-Cancer Association-Genitourinary Oncology Committee. |
| Dr. Thomas Herzog | He is a deputy director of the University of Cincinnati Cancer Institute and professor of Obstetrics and Gynecology at the UC College of Medicine. |
| Dr. William Edenfield | He is a hematology and oncology specialist based in Greenville, Carolina and has approximately 30 years of experience in the medical field. He graduated from the University of Miami Miller School of Medicine in 1992. |
| Dr. Lingying Wu (吳令英) | She is the director of the Department of Gynecologic Oncology of Cancer Hospital of Chinese Academy of Medical Sciences, the executive standing committee member of the Clinical Oncology Collaborative Center of Chinese Anti-Cancer Association and a member of the Gynecologic Oncology Specialty Committee. |
| Dr. Lin Shen (沈琳) | She is the director of the Department of Gastrointestinal Oncology of Peking University Cancer Hospital. |
| PI B | He is a member of the Chinese Academy of Engineering, the director of the National Clinical Research Center for New Drugs (Anti-tumor), and the 6th Academic Committee of the National Cancer Center. |
| Dr. Sneha Phadke | She is a clinical associate professor of internal medicine-hematology, oncology, and blood and marrow transplantation in the University of Iowa Health Center. |

*Translational Research*

We conduct pre-clinical and clinical translational research to assess the effects of our drug candidates in specific group of patients. The patients can often be defined as presence or absence of a biomarker, or progressed after certain drug treatment. This translational research can greatly help our clinical trial design and make the best uses of a drug on patients who will receive the most benefits. These insights help further guide us toward new directions in drug discovery and efficiently obtain proof of concept results. We also maintain extensive collaboration with physicians, scientists and key opinion leaders, and further develop products based on their clinical feedback to our drug candidates, whether in terms of indications or potential treatment combinations. We have established a rich network of top-tier CROs, SMOs, research institutions and hospitals so that our drug candidates can be quickly moved to the clinical stage.

*Collaboration with CRO Partners (including both CROs and SMOs)*

We collaborate with CRO partners (including both CROs and SMOs) to conduct and support our pre-clinical and clinical studies in line with industry practice. We select our CRO partners by weighing various factors, such as their qualifications, academic and professional experience, industry reputation and service fees. To the best of our Company's knowledge, none of them has any past or present relationships with our Group, our Directors, shareholders, senior management or any of their respective associates.

The pre-clinical CRO partners mainly provide us with services related to pre-clinical toxicity and safety evaluations, such as animal studies, of our drug candidates in accordance with our study design and under our supervision. The clinical CRO partners provide us with an array of services necessary for complex clinical trials in accordance with our trial design and under our supervision. CRO partners generally provide a comprehensive suite of services to assist us with implementing and managing clinical trials, including trial preparation, source data verification, clinical safety management, data management, and report preparation. We choose to engage a CRO partner based on the complexity and workload of a specific trial. We closely monitor the work of our CRO partners and provide specific directions to ensure the quality and efficiency of the trial execution. This approach allows us to leverage the experience of our in-house team to better focus on critical clinical trial elements, such as trial design, data analysis and decision making. All studies of our drug candidates on humans are conducted in compliance with the applicable laws, regulations and in line with the industry standards. We believe our ability to conduct and work closely with CRO partners to conduct pre-clinical studies and clinical trials enables us to shorten the time required for drug development by generating the requisite data reliably and efficiently.

The following table sets forth background of our major CRO partners and expenses attributable thereto during the Track Record Period:

| | Background | For the Year Ended December 31, 2021 | For the Year Ended December 31, 2022 | Total Amount during the Track Record Period |
|---|---|---|---|---|
| | | *RMB'000* | *RMB'000* | *RMB'000* |
| **CRO Partners** | | | | |
| CRO A | It is headquartered in the U.S. and was founded in 2014. It conducts clinical trials on behalf of its pharmaceutical clients to expedite the drug approval process. | 20,533 | 19,465 | 39,998 |
| GOG Foundation, Inc. | It is headquartered in the U.S. and was founded in 1970. It is an organization that provides services in clinical trials and research in the field of gynecologic malignancies. | 7,769 | 24,250 | 32,019 |
| CRO B | It is headquartered in the U.S. and was founded in 1982. It provides biopharmaceutical development and commercial outsourcing services, focused primarily on Phase I-IV clinical trials and associated laboratory and analytical services. It is a company listed on the New York Stock Exchange. | 15,227 | 12,767 | 27,994 |
| CRO C | It is headquartered in Shanghai and was founded in 2010. It provides non-clinical safety evaluation, non-clinical pharmacokinetic studies, preclinical and clinical biomarker analysis and drug application consulting services. | – | 15,648 | 15,648 |
| CRO D | It is headquartered in Shanghai and was founded in 2016. It is a clinical development partner, committed to enable customers to accelerate the delivery of innovative solutions to patients worldwide. | 6,125 | 3,520 | 9,645 |
| **Total** | | 49,654 | 75,650 | 125,304 |

In 2021 and 2022, the expenses related to CRO partners included in our research and development expenses were RMB76.5 million and RMB121.0 million, respectively. We mainly determine the service fees related to the CRO partners in accordance with the then prevailing market prices of similar services, the number of enrolled patients, the duration of the clinical trials, the number of service cycles, the number of centers monitored and the quality and contents of the services provided.

**Chemistry, Manufacture & Controls and Manufacturing**

***CMC Team***

Our chemistry, manufacture and control (CMC) team is led by Dr. Tao Feng, who is experienced in drug development and manufacturing for various products. As of the Latest Practicable Date, our CMC team consists of six professionals with established experience in process development, production and quality management from well-known biopharmaceutical and pharmaceutical companies. Our CMC team is responsible for (i) process development, scale-up, optimization, characterization and validation; (ii) analytical method development and validation; and (iii) clinical drug manufacturing and commercial product launching.

***Collaboration with CDMO Partners (including both CMOs and CDMOs)***

We collaborate with our CDMO partners (including both CMOs and CDMOs) to manufacture a portion of our drug candidates to supply for pre-clinical studies, clinical trials and potentially for the commercial-scale production of large molecule drugs. Our CDMO partners are usually companies that primarily engage in the development and manufacturing of drugs. We select our CDMO partners based on their operating history, market reputation, relevant expertise, internal quality control system, production technology, cGMP certification, production capacity, and pricing. To the best of our Company's knowledge, none of them has any past or present relationships with our Group, our Directors, shareholders, senior management or any of their respective associates, and the CMOs and CDMOs engaged by us are Independent Third Parties. We did not experience material product quality issues in respect of the products manufactured by our CDMO partners during the Track Record Period. We believe that other alternative CDMO partners can meet our quality standards at comparable prices.

Under our agreement with our CDMO partners, they are required to perform services according to the prescribed time frame as set out in the agreement. Usually, we pay the CDMO partners in a lump sum with a short credit period. Our CDMO partner is responsible for manufacturing our required products in accordance with certain product specifications, in compliance with cGMP requirements and our quality standards. We retain all the intellectual property rights and grant our CDMO partner the right to use our intellectual property rights for such manufacturing and packaging activities during the contract period. We are entitled to inspect and audit our CDMO partner's manufacturing process. Our CDMO partner is also required to acquire and maintain all relevant permits and certificates. If our CDMO partner fails to deliver products or comply with substantial obligations under the relevant agreement, we are entitled to terminate the agreement or reduce our order amount. Our CDMO partner receives processing fees from us according to a price schedule in the agreement, which sets per unit fees for respective production volumes.

The following table sets forth background of CDMO partners and expenses attributable thereto during the Track Record Period:

| | Background | For the Year Ended December 31, 2021 | For the Year Ended December 31, 2022 | Total Amount during the Track Record Period |
|---|---|---|---|---|
| | | *RMB'000* | *RMB'000* | *RMB'000* |
| **CDMO Partners** | | | | |
| CDMO A | It is headquartered in Jiangsu and was founded in 2000. It provides a broad portfolio of R&D and manufacturing services that enable its pharmaceutical and healthcare industry clients to advance discoveries and deliver treatments to patients. It is a company listed on the Hong Kong Stock Exchange and the Shanghai Stock Exchange. | 27,721 | 80,430 | 108,151 |
| HALO PHARMACEUTICAL, INC. D/B/A CAMBREX WHIPPANY | It is headquartered in the U.S. and was founded in 1981. This leading small molecule CDMO provides drug substance, drug product, and analytical services across the entire drug lifecycle. | 7,475 | 8,325 | 15,800 |
| CDMO B | It is headquartered in Shanghai and was founded in 2014. It is a cloud supply chain platform for pharmaceutical R&D industry with SaaS-based e-commerce services, consumables and instruments procurement integration. Its service scope covers the whole life cycle of pharmaceutical research and development. | 1,927 | 3,721 | 5,648 |
| CDMO C | It is headquartered in the U.S. and was founded in 2007. It is is the global leader in enabling pharma, biotech, and consumer health partners to optimize product development, launch, and full life-cycle supply for patients around the world. | 1,046 | 994 | 2,040 |
| CDMO D | It is headquartered in Italy and was founded in 2006. It is one of the leading CDMOs focused on development, clinical and commercial production and fully dedicated to anticancer drugs. | – | 1,434 | 1,434 |
| **Total** | | 38,169 | 94,904 | 133,073 |

In 2021 and 2022, the expenses related to CDMO partners included in our research and development expenses were RMB42.6 million and RMB98.3 million, respectively. We mainly determine the service fees related to the CDMO partners in accordance with the then prevailing market prices of similar services, the number of enrolled patients, the duration of the clinical trials, the number of products manufactured, and the quality and contents of the services provided.

***Manufacturing Facilities***

To support future commercial manufacturing of our small molecule products, we plan to construct a new oral solid dosage manufacturing facility in eastern China. Our site is designed to comply with the cGMP requirements of the NMPA, EMA and FDA. Our manufacturing capacity and production lines will be inter-changeable among the products. We expect that the completed manufacturing facility will be able to support our commercialization needs in China and overseas for the next three years. In the future, we may expand or add additional manufacturing facilities to meet our commercial needs.

LAE002, the drug candidate that we expect to first commercialize, will be initially manufactured by CDMOs upon marketing approval and later transferred to our own manufacturing facility upon approval by competent regulatory authority.

**Quality Assurance and Control**

As of the Latest Practicable Date, our quality assurance and control is led by an industry veteran with about 15 years of industry experience. Our quality assurance ensures that our suppliers deliver products in accordance with our product quality requirements and current GMP regulations through protocols specifying quality guarantees, manufacturing site monitoring and regular supplier evaluations.

**Regulatory Affairs**

Our regulatory affairs team is responsible for the regulatory approval process of our drug candidates, including assembling application dossiers for IND and NDA, addressing inquiries from relevant authorities and monitoring our R&D projects to ensure their compliance with relevant regulations. Our regulatory affairs team manages the regulatory submission process for our drug candidates, which requires filings to be made to and approved by the relevant authorities before clinical trials and commercialization can be initiated. The regulatory affairs team prepares and manages regulatory filings by drafting filing dossiers, addressing regulatory questions and conducting CMC and GMP readiness assessments for our drug candidates. We possess extensive knowledge and experience with regard to regulatory filings in China and the U.S. With our presence and expertise in both the U.S. and China, we can design our clinical trials to maximize operational efficiency.

## Commercialization

We plan to adopt localized commercialization strategies for both domestic and overseas markets. As of the Latest Practicable Date, we had 92 employees in total, including 82 employees in China and 10 employees in the U.S. For the domestic market, we plan to partner with principal investigators with substantial industry influence and expertise, publish our clinical trial results in academic conferences and journals for physician education, recruit market analysts and product promotion specialists to tailor commercializing strategies for each of our Core Products, engage distributors that have broad hospital coverage, and assemble a full-fledged in-house commercialization team with expertise in medical, sales and marketing, regulatory and supply chain areas. In particular, considering the fierce competition in China's oncology drug market, we plan to work with competent local partners for commercialization, and leverage their sales channels for marketing. We also plan to adopt a tiered provincial market-entry approach with the goal of achieving nationwide coverage in the medium term. Our priority is to initially focus on top tier provinces that have favorable reimbursement coverage and high patient volume. As we expand into tier two and lower tier provinces, we plan to continue to invest in building our on-the-ground presence and coverage. We will seek to strengthen our relationship with key stakeholders in each province to drive diagnosis and treatment, and also to support reimbursement negotiation into provincial formulary. We believe these marketing and business development strategies will help us obtain market shares in the indications that we focus on. For the overseas market, we plan to partner with local pharmaceutical companies to utilize their local sales networks and other resources to achieve mutually beneficial results and maximize the commercial value of our Core Products.

### *Pricing, Tendering and Reimbursement Strategies*

During the Track Record Period and up to the Latest Practicable Date, we had not commercialized any of our Core Products. We have not yet formulated any definitive pricing policy for our Core Products. When our Core Products progress to commercialization in the future, we will determine their prices based on various factors such as our Core Products' advantages, costs, the prices of competing products, and if they are to be included into the National Reimbursement Drug List (NRDL), the NRDL's reference price. We plan to conduct extensive market research with KOLs, hospitals, physicians and patients as well as regulatory agencies before pricing our Core Products, and intend to take into account various factors such as feedback collected from these parties, our production costs, the differences in safety and efficacy profiles, the estimated demand for our Core Products, and the clinical value we bring to the patients to price our Core Products.

In order to gain market share against existing and future branded and generic competitors, we will also consider seeking inclusion of our Core Products into the NRDL and other reimbursement programs. Inclusion into the NRDL is evaluated and determined by the relevant government authorities and we may face significant competition for successful inclusion. While products included in the NRDL or the PRDL are typically generic and essential drugs, many innovative drugs have been included in the NRDL in the past. Although we believe that the Core Products are eligible for inclusion upon commercialization and meeting NRDL's criteria, if we fail to have our Core Products included in the NRDL after commercialization, our sales channels may be limited and our revenue from commercial sales will be highly

dependent on patient self-payments, which could make our products less competitive. We may need to seek alternatives such as commercial private insurance coverage of LAE001 and LAE002 and need to expand our sales channels and explore new collaboration partnerships, such as engaging distribution partners in China, to maximize the sales potential of our products and enhance our commercialization capability, especially on customer reach. We also plan to expand our sales network by closely communicating with physicians, especially KOLs in renowned comprehensive hospitals through clinical trial cooperation and other academic activities. As we expand our portfolio, we believe we will be well-positioned to leverage our existing sales network to rapidly launch and commercialize our new products.

We have built an extensive patent portfolio to protect each of our drug candidates, including in relation to their structure, treating method/use, combination and others. Although patents related to composition of matter of LAE002 or LAE003 may expire in 2028, we plan to apply patent term extension for LAE002 or LAE003 to extend the patent term in China, the U.S. and other jurisdictions. Additionally, other patents relating to the drug candidate or product at issue such as methodology, usage or formulation patents may continue to protect our exclusivity in developing and commercializing them. Although generic competitors of LAE002 and LAE003 are currently not available, upon the expiration of relevant patents, we may face fierce competition from generic or biosimilar products, including from the ATK inhibitors in generic or biosimilar form of LAE002 and LAE003, which may have a negative impact on the commercialization of LAE002 and LAE003 and our financial position. In addition to the above commercialization strategy efforts, we may seek to optimize our profits by introducing our own generic drugs before the relevant patents expire.

Additionally, we plan to build a dedicated in-house sales and marketing team to cover the market in China. Our initial target is to create, at the time of the commercialization of LAE002, a sales team of approximately 60 people to cover approximately 50 of the top hospitals in China, which are equipped with the technology and physicians to administer our LAE002. In particular, we plan to set up sales and operations teams at the target hospitals to facilitate the use of our products. These teams will ensure our LAE002 are administered in accordance with the applicable standards and provide advice to the hospital staff. As our business grows over the next three years, we anticipate expanding our sales force to approximately 100 people in order to support the administration of our LAE002 across the top 100 oncology hospitals in China. For the commercialization of LAE003, we plan to collaborate with partners for its development and commercialization overseas.

## BUSINESS DEVELOPMENT

To support our long-term business strategy and to fulfill the potential of our company's assets, our corporate and business development group advances a holistic approach to continuously assess partnering opportunities with various global and regional stakeholders in the biopharmaceutical and biotech industry. These opportunities may include co-developments of new treatment modalities for our existing clinical stage pipeline in order to deliver additional solutions for patients. Additionally, as part of our core strategy to develop innovative drugs to market, we continue to seek research partnerships, in the pursuit to bring in house cutting edge science and technologies in the field of drug development for cancer and liver diseases.

Our R&D team collaborates closely with our corporate and business development group to evaluate business opportunities to optimize our pipeline structure in accordance with our product development strategy and R&D principles. Leveraging our understanding and scientific insights into cancer disease biology, especially the PI3K/AKT/mTOR pathway, we have successfully acquired from Novartis four clinically validated assets with strong combinatorial potential in solid tumors, spearheaded by LAE002 and LAE001.

We have a proven track record of success partnering with global pharmaceutical and biotechnology companies across our pipeline, and we continue to manage those alliances and transform them into success stories. We understand the importance of the network we have built to drive our strategic focus forward. Therefore, we continue to engage with external resources for innovation and growth that will transform our efforts to a commercial success.

## INTELLECTUAL PROPERTY

Intellectual property rights are central to the success of our business. Our commercial future will depend, in part, on our ability to acquire and protect our intellectual property rights for commercially significant technologies, inventions and know-how. This includes acquisition of new patents, defense of existing patents, and protection of our trade secrets. We will also have to operate without infringing, misappropriating, or otherwise violating third parties' valid, enforceable intellectual property rights.

As of the Latest Practicable Date, we held 174 patents and patent applications (including in-licensed patents and patent applications with global rights), among which 145 patents and patent applications of our drug candidates were in-licensed from Novartis AG. The following table sets forth an overview of our material granted patents and filed patent applications in connection with our clinical and pre-clinical drug candidates as of the Latest Practicable Date:

| Product | Subject Matter of Patent Family[1] | Jurisdiction | Status | Applicant/Assignee | Expected Patent Expiration[2] | Market Commercial Rights of the Company |
|---|---|---|---|---|---|---|
| LAE002/LAE003 | Composition of matter | U.S. | issued | Novartis AG | 2031 | exclusive license rights |
| | | Argentina, Australia, Brazil, Canada, mainland China, EPO (Austria, Belgium, Denmark, France, Germany, Greece, Hong Kong, Ireland, Italy, Netherlands, Poland, Portugal, Spain, Sweden, Switzerland, Turkey, UK), India, Israel, Japan, South Korea, Mexico, Singapore, South Africa | issued | Novartis AG | 2028 | exclusive license rights |

| Product | Subject Matter of Patent Family[1] | Jurisdiction | Status | Applicant/Assignee | Expected Patent Expiration[2] | Market Commercial Rights of the Company |
|---|---|---|---|---|---|---|
| | Combinations for treating cancer and use thereof | Japan | issued | Novartis AG | 2034 | exclusive license rights |
| | | U.S., mainland China, EPO, Hong Kong, Japan | pending | Novartis AG | 2034 | exclusive license rights |
| | Enzalutamide in combination with afuresertib for the treatment of cancer | Mainland China, EPO (France, Germany, UK), Japan | issued | Novartis AG | 2034 | exclusive license rights |
| LAE002 | Crystalline N-{(1)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1h-pyrazol-5-yl)-2-thiophenecarboxamide hydrochloride | U.S. | issued | Novartis AG | 2031 | exclusive license rights |
| | | Australia, Brazil, Canada, mainland China, Israel, Japan, South Korea, Mexico, Singapore, South Africa, Kazakstan | issued | Novartis AG | 2030 | exclusive license rights |
| | | EPO, Hong Kong | pending | Novartis AG | 2030 | exclusive license rights |
| | Combination of bortezomib with afuresertib and use thereof in the treatment of cancer | U.S., mainland China, EPO (France, Germany, UK), Japan | issued | Novartis AG | 2032 | exclusive license rights |
| LAE001 | Composition of matter | U.S. | issued | Novartis AG | 2031 | exclusive license rights |
| | | Australia, Brazil, Canada, mainland China, EPO (Austria, Belgium, France, Germany, Greece, Italy, Netherlands, Poland, Portugal, Spain, Switzerland, Turkey, UK), India, Japan, South Korea, Mexico | issued | Novartis AG | 2030 | exclusive license rights |
| LAE005 | Antibody molecules to PD-L1 and uses thereof | U.S. | issued | President & Fellows of Harvard College; Dana Farber Cancer Inst. Inc.; Novartis AG | 2036 | exclusive license rights |
| | | Australia, mainland China, Israel, Japan, Mexico, Macao, EPO (France, Germany, Italy, Spain, UK), South Korea | issued | President & Fellows of Harvard College; Dana Farber Cancer Inst. Inc.; Novartis AG | 2035 | exclusive license rights |

| Product | Subject Matter of Patent Family[1] | Jurisdiction | Status | Applicant/Assignee | Expected Patent Expiration[2] | Market Commercial Rights of the Company |
|---|---|---|---|---|---|---|
| | | U.S., Brazil, Canada, mainland China, Hong Kong, India, Japan, Singapore, South Africa | pending | President & Fellows of Harvard College; Dana Farber Cancer Inst. Inc.; Novartis AG | 2035 | exclusive license rights |
| | Dosage regimens for anti-PD-L1 antibodies and uses thereof | U.S., mainland China, EPO, Japan, Hong Kong | pending | Novartis AG | 2039 | exclusive license rights |
| Combination of LAE002 and LAE001 | Method of treating cancer | U.S., Australia, Brazil, Canada, mainland China, Eurasia, EPO, Israel, Japan, South Korea, Mexico, Singapore, South Africa, Hong Kong | pending | Our Company | 2040 | ownership |
| Combination of LAE002 and LAE005 | Combination of afuresertib and an anti-PD-L1 mAb | PCT | pending | Our company | 2043 | ownership |
| LAE104/LAE105 | Depletion of activated hepatic stellate cells (HSCs) | PCT | pending | Our Company | 2042 | ownership |
| LAE102 | Anti-ACVR2A antibodies and uses thereof | PCT | pending | Our Company | 2042 | ownership |
| LAE111 | Anti-lilrb1 and/or anti-lilrb2 antibodies and uses thereof | PCT | pending | Our Company | 2043 | ownership |
| LAE118 | Multicyclic compounds and their use as PI3Kα inhibitors | PCT | pending | Our Company | 2043 | ownership |
| LAE119 | Fused multicyclic compounds and their use as PARP1 inhibitors | PCT | pending | Our Company | 2042 | ownership |
| LAE120 | Fused bicyclic compounds and their use as USP1 inhibitors | PCT | pending | Our Company | 2042 | ownership |
| | Heteroaromatic compounds and their use as USP1 inhibitors | PCT | pending | Our Company | 2043 | ownership |

*Abbreviations: EPO = European Patent Office; UK = United Kingdom; U.S. = United States; PCT = Patent Cooperation Treaty.*

*Notes:*

(1) Unless otherwise indicated, the patent for applications within the same family is the same and is therefore disclosed once.

(2) The expected patent expiration date is estimated based on current filing status on the assumption that a patent is granted to a pending application, without taking into account any possible patent term adjustments or extensions except as noted for the U.S. patents, the expiration date of which takes into account the patent term adjustments and terminal disclaimers as shown in the U.S. Patent and Trademark Office database, assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

The term of individual patents may vary based on the countries in which they are obtained. In most countries and regions in which we file patent applications, the term of an issued patent is generally 20 years from the filing date of the formal patent application on which the patent is based in the applicable country or region. 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 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.

The actual protection provided by a patent varies on a claim-by-claim and country-by-country basis and depends upon various factors, including the type of patent, the scope of its coverage, the availability of any patent term extensions or adjustments, the availability of legal remedies in a particular country or region, and the validity and enforceability of the patent. We cannot provide any assurance that patents will be issued with respect to any of our owned or licensed pending patent applications or any such patent applications that may be filed in the future, nor can we provide any assurance that any of our owned or licensed issued patents or any such patents that may be issued in the future will be commercially useful in protecting our product candidates and methods of manufacturing the same.

We have not obtained patent protections for some early-stage drug candidates because (i) more efforts are needed to complete the design of molecular structure of the drug candidates and to evaluate the characteristics, functions and effects of the drug candidates; and (ii) the submitted patent applications are currently in prosecution of patent office. As of the Latest Practicable Date, amongst our non-patented drug candidates, LAE102, LAE104, LAE105, LAE111, LAE118, LAE119 and LAE120 patent applications have been submitted to patent offices in major markets, and have been accepted for prosecution. For LAE106, LAE109, LAE113, LAE117, and LAE112, once we have determined the molecular structure for the final drug candidates to the clinical studies, we will file patent applications in China, U.S. and other relevant jurisdictions promptly. We also plan to set up patent portfolios to provide extensive patent protections.

We may rely, in some circumstances, on trade secrets and confidential information to protect aspects of 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, certain key members of our R&D team, and other employees who have access to trade secrets or confidential information about our business. Our standard employment contract, which we use to employ each employee, contains an assignment clause. We own all the rights to all inventions, technology, know-how, and trade secrets derived during such employees' employment.

These agreements may not sufficiently protect our trade secrets and confidential information. These agreements may also be breached, resulting in the misappropriation of our trade secrets and confidential information, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and 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 obtain or use information that we regard as proprietary without our consent. As a result, we may not 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 the physical security of our premises and the 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. See "Risk Factors – Risks Relating to Our Intellectual Property Rights" to describe risks related to our intellectual property.

We conduct our business under the brand name "LAEKNA". As of the Latest Practicable Date, we had registered 17 trademarks in mainland China and Hong Kong. We are also the registered owner of three domain names.

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

## SUPPLIERS

During the Track Record Period, we primarily procured services and raw materials to develop our drug candidates from highly reputable manufacturers and suppliers. Our purchases mainly include third-party contracting services for pre-clinical evaluation and clinical trials of our drug candidates, raw materials, and consumables. Our purchases from our five largest suppliers in the aggregate in each period during the Track Record Period amounted to RMB78.7 million and RMB152.6 million, representing 63.4% and 67.2% of our total purchases (excluding value-added tax), respectively. Our purchases from our largest supplier in each period during the Track Record Period amounted to RMB27.7 million and RMB80.4 million, representing 22.3% and 35.4% of our total purchases (excluding value-added tax), respectively.

To the best of our knowledge, all of our five largest suppliers during the Track Record Period are Independent Third Parties. None of our Directors, their respective 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, has any interest in any of our five largest suppliers during the Track Record Period.

In addition, we believe that adequate alternative sources for such supplies exist, and we have developed alternative sourcing strategies for these supplies. We will establish necessary relationships with alternative sources based on supply continuity risk assessment. We generally have credit periods of 30 days.

Below is a summary of the key terms of a typical agreement with our CROs, SMOs and CDMOs.

- *Services*. The CRO, SMO, or CDMO provides us with services such as implementing a clinical research project, manufacturing products as specified in the master agreement or work order.

- *Term*. The CRO, SMO or CDMO is required to perform its services according to the prescribed timeframe set out in the master agreement or a work order.

- *Payment*. We are required to make payments to the CRO, SMO, or CDMO according to the payment schedule agreed by the parties.

- *Confidentiality.* We and the CRO, SMO or CDMO agree to keep confidential any information in relation to the performance of the master agreement.

- *Intellectual Property.* We own all intellectual property derived from the clinical research project, and we are entitled to apply patent for such intellectual properties.

The tables below set forth certain information about our five largest suppliers in terms of total purchases during the Track Record Period:

**For the Year Ended December 31, 2021**

| Supplier | Years of Relationship | Credit Term | Product or Service Supplied | Purchase Amount *(RMB'000)* | Percentage of Total Purchases |
|---|---|---|---|---|---|
| Supplier A (CDMO A) | Since 2018 | 30 days | CDMO service, pre-clinical research service, clinical research coordinator service | 27,721 | 22.3% |
| Supplier B (CRO A) | Since 2019 | 30 days | CRO service | 20,533 | 16.5% |
| Supplier C (CRO B) | Since 2018 | 30 days | CRO service | 15,227 | 12.3% |
| Supplier D | Since 2019 | 30 days | Clinical research service | 7,769 | 6.3% |
| Supplier E | Since 2019 | N/A | CDMO service | 7,475 | 6.0% |

| | For the Year Ended December 31, 2022 | | | | |
|---|---|---|---|---|---|
| **Supplier** | **Years of Relationship** | **Credit Term** | **Product or Service Supplied** | **Purchase Amount** *(RMB'000)* | **Percentage of Total Purchases** |
| Supplier A (CDMO A) | Since 2018 | 30 days | CDMO service, pre-clinical research service, clinical research coordinator service | 80,430 | 35.4% |
| Supplier D | Since 2019 | 30 days | Clinical research service | 24,250 | 10.7% |
| Supplier B (CRO A) | Since 2019 | 30 days | CRO service | 19,465 | 8.6% |
| Supplier F (CRO C) | Since 2021 | 30 days | Pre-clinical research service | 15,648 | 6.9% |
| Supplier C (CRO B) | Since 2018 | 30 days | CRO service | 12,767 | 5.6% |

## COMPETITIONS

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, competition and a strong emphasis on proprietary drugs. While we believe our pipeline of clinical and pre-clinical stage proprietary assets, leading R&D capability, biopharmaceutical platform and seasoned management team provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, and public and private research institutions.

We primarily focus on the research and development of small molecule targeted oncology therapies, in particular, our Core Products, LAE001 (anti-CYP17A1 androgen synthesis inhibitor) and LAE002 (AKT inhibitor). Although no AKT inhibitor has been approved for commercialization yet, seven AKT inhibitors are under clinical development globally, focusing on the treatment of a variety of solid tumors such as ovarian cancer and breast cancer. For anti-androgen drugs, there are seven anti-androgen drugs approved for commercialization globally (ex-China) and seven anti-androgen drugs approved in China. There are 11 anti-androgen drugs in clinical trials globally and five anti-androgen drugs in clinical trials in China.

We also face potential competition from existing drug products and drug product candidates under development even though they may be of different classes as well as conventional treatment therapies in the entire oncology market. Although the field of cancer treatment has developed significantly in the past decade, conventional treatment methods such

as surgery, radiotherapy and chemotherapy are still been widely used to treat cancer. Alternative treatments such as targeted oncology and immuno-oncology are generally used only if other therapy options are not suitable or effective on patients. See "Industry Overview" for more details on the competitive landscape of the various markets in which we compete.

## GOVERNMENT GRANTS, AWARDS AND RECOGNITIONS

We have received a wealth of grants and awards. Major government grants that we had received as of the Latest Practicable Date are set forth in the table below.

| Year | Grant Type | Project Name | Project Level |
|---|---|---|---|
| 2021 | Subsidies for science and technology projects | Shanghai Science and Technology Commission Innovative Product Tackling Project (上海市科學技術委員會創新產品攻關項目) | Provincial |
| 2020 | Subsidies for science and technology projects | Zhangjiang High-Tech Park Support for innovation and entrepreneurship environment (張江科學城支持創新創業環境細則政策) | Provincial |

The following table sets forth some of the important accreditations and awards we had received from the relevant authorities and organizations in China as of the Latest Practicable Date in recognition of our research and development capabilities:

| Year | Accreditation/Award | Accreditation Organization |
|---|---|---|
| 2022 | 2022 China Pharmaceutical Seed Enterprise Innovation Top 100 (2022中國醫藥種子企業創新100強) | Healthcare Executive (E藥經理人) |
| 2022 | 2022 Pioneers: The Scientists (科學家創業先鋒榜) | www.chinastarmarket.cn (科創版日報) |
| 2022 | China Future 50 – Biotech (中國生物科技創新50企業) | KPMG (畢馬威) |
| 2021 | 2021 China CSR Cloud Summit "Excellent Case of Social Responsibility" (2021中國企業社會責任雲峰會"社會責任優秀案例") | www.xinhuanet.com (新華網) |

| Year | Accreditation/Award | Accreditation Organization |
|---|---|---|
| 2021 | 2021 China Sci-Tech Good Company Biomedical Pioneer-10 (2021中國科創好公司,生物醫療Pioneer-10) | www.chinastarmarket.cn (科創版日報) |
| 2021 | 2021 China Pharmaceutical Seed Enterprise Innovation Top 100 (2021中國醫藥種子企業創新100強) | Healthcare Executive (E藥經理人) |
| 2021 | 2021 R&D Frontier Award (2021年度研發前沿獎) | Pharma DJ (研發客) |
| 2021 | Top 100 Most Powerful Companies with Technology Top 50 Most Powerful Innovative Companies with Technology (最具科技力量百強企業榜,最具科技力量創新企業TOP50) | Frost & Sullivan |
| 2020 | The First Tumor Treatment High Technology Conference – and Annual Top 20 of Tumor Treatment High Technology (首屆腫瘤診療黑科技大會–暨腫瘤診療黑科技年度TOP20) | Liangyihui (良醫匯) and CSCO Foundation (北京市希思科臨床腫瘤學研究基金會) |
| 2019 | China Medical Health Industry Investment and Financing Glory List – Top 20 Best Newcomer Award in Medical Health Industry (中國醫療大健康產業投融資榮耀榜–醫療健康產業最佳新銳獎TOP20) | CHC Consultant (CHC醫療傳媒) and CITIC Securities (中信證券) |
| 2018 | Insight Zhangjiang Top 100 (洞見張江TOP100) | Zhangjiang Venture (張江科投) and JingData (鯨準) |

## INSURANCE

We maintain insurance policies that we consider to be in line with market practice and adequate for our business. Our principal insurance policies cover employee benefits liability and adverse events in clinical trials. We currently do not maintain insurance for environmental liability or property loss. Please refer to the section headed "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 92 employees in total. Among the 92 employees, 71 are stationed in our headquarters in Shanghai. The following table sets forth the number of our employees categorized by function as of the Latest Practicable Date.

| Function | Number | Percentage of Total |
|---|---|---|
| Research and Development | 58 | 63.0% |
| CMC and Quality | 7 | 7.6% |
| Business Development | 2 | 2.2% |
| Operations | 25 | 27.2% |
| **Total** | 92 | 100% |

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, 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 provide continuing education and training programs, including internal training, to improve their technical, professional or management skills. 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. Furthermore, we provide various incentives and benefits to our employees, including competitive salaries, bonuses and share-based compensation, particularly our key employees.

Our employees' remuneration comprises salaries, bonuses, provident funds, social security contributions, and other welfare payments. We have made contributions to our employees' social security insurance funds (including pension plans, medical insurance, work-related injury insurance, unemployment insurance and maternity insurance) and housing funds pursuant to applicable laws and regulations. We have complied with all statutory social security insurance fund and housing fund obligations applicable to us under the laws and regulations in China in all material aspects during the Track Record Period and as of the Latest Practicable Date. Please refer to the section headed "Risk Factors – Risks Relating to Doing Business in China – Failure to comply with relevant regulations relating to social insurance and housing provident fund may subject us to penalty" in this document.

## LAND AND PROPERTIES

As of the Latest Practicable Date, we do not own any real property. As of the Latest Practicable Date, we leased four properties in China with an aggregate GFA of approximately 5,493.3 sq.m. We believe our current facilities are sufficient to meet our near-term needs, and additional space can be obtained on commercially reasonable terms to meet our future needs. We do not anticipate undue difficulty in renewing our leases upon their expiration.

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

| **Usage** | **Location** | **GFA** *(sq.m)* | **Lease Term** |
|---|---|---|---|
| Office and laboratory | Shanghai | 1,261.1 | September 16, 2021 to September 15, 2027 |
| Office | Beijing | 60 | September 1, 2022 to August 31, 2023 |
| R&D | Shanghai | 4,042.2 | August 10, 2021 to November 30, 2030 |
| Office | Shanghai | 130 | March 28, 2022 to March 31, 2023; (Renewed) April 1, 2023 to March 31, 2024 |
| Office | Los Angeles, United States | N/A* | December 1, 2022 to November 30, 2023 |

*Note:*

* In the U.S., we entered into a membership agreement with 10250 Constellation Tenant LLC ("WeWork") for the capacity of five memberships for our office operation.

## ENVIRONMENTAL, SOCIAL, AND GOVERNANCE

### Governance

We acknowledge our environmental protection and social responsibilities and are aware of the climate-related issues that may impact our Group's business operation. We are committed to complying with environmental, social and governance ("**ESG**") reporting requirements upon [**REDACTED**].

We have established a set of ESG policies covered under relevant international standards. We endeavor to reduce negative impacts on the environment through our commitment to energy saving and sustainable development. For environmental matters, we have adopted policies related to (i) reduction of greenhouse gas emissions, (ii) treatment of exhaust gas and solid waste, (iii) adoption of materials that cause minimum environmental concerns to the extent possible, and (iv) conservation of energy, among other aspects. We continue to promote work-life balance and create a positive workplace for all of our employees. For social matters, we have adopted policies related to (i) product quality and clinical trial safety, (ii) employee health, promotion, compensation and benefits, (iii) employee training, wellness and professional and personal development, and (iv) employee complaint handling, among other aspects.

Our ESG policies also sets out different parties' respective responsibilities and authority in managing the ESG matters. Our Board has overall responsibility for overseeing and determining our Group's environmental, social, and climate-related risks and opportunities impacting our Group, establishing and adopting the ESG policy and targets of our Group, and reviewing our Group's performance annually against the ESG targets and revising the ESG strategies as appropriate if significant variance from the target is identified.

Our Company [has established] an ESG committee, see "Directors and Senior Management – Corporate Governance – ESG Committee" for details.

### Potential Impacts of ESG-Related Risks

We do not conduct manufacturing activities, thus generate no direct emissions and industrial wastes. However, we are subject to various ESG related laws and regulations in China, and our operations are regularly inspected by local government authorities. For further details, please refer to "Regulatory Overview – Regulations on Environmental Protection and Fire Prevention" in this document.

During the Track Record Period and up to the Latest Practicable Date, we have 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.

In view of the nature of our business, to the best knowledge of our Directors, the climate change will not have any major impact on our business operation. In the case of extreme natural weather, we will actively respond to the relevant policies of local government, make contingency plans in addition to the life insurance contributed by our Group to ensure the safety of our staff. In the case of acute physical risks such as direct damage to assets and indirect impacts from supply chain disruption as a result of extreme weather events, we will make corresponding contingency and disaster preparedness plans, and we believe that we have the ability to deal with climate crisis. During the Track Record Period and up to the Latest Practicable Date, we had not experienced any material impact on our business operations, strategies or financial performance as a result of environmental, social and climate-related issues.

Potential transition risk may result from a lower-carbon economy, which entails climate-related regulations and policy change and reputational risk. Currently, the National Development and Reform Commission and the Ministry of Ecology and Environment have jointly issued the Opinions on Further Strengthening the Cleanup of Plastic Pollution, laying out a five-year roadmap to restrict the use, production and sale of plastic products by 2020, 2022, and 2025, respectively. Our Group will work with the suppliers to comply with such regulations, and we will monitor the scope to ensure our works meet the expectations of the regulators.

| | **Risks** | **Potential Impacts** |
|---|---|---|
| **Short term (current annual reporting period)** | • Extreme weather conditions such as flooding and storms<br>• Sustained elevated temperature | • Reduced revenue from damage to assets, disruption to third-party logistic providers or third-party manufacturers |
| **Medium term (one to three year)** | | • Increased operating expenses |
| **Long term (four to ten years)** | • Change in climate-related regulations<br>• Shifts in customer preferences | • Reduced demand for goods and services |

**Strategies in Addressing ESG-Related Risks**

We have adopted various measures in managing the air emissions and greenhouse gas ("**GHG**") emissions during our operations, including but not limited to:

- requiring employees to turn off lights, equipment, and other electronic devices when the devices are not in operation and before they leave the premises;

- using more energy-efficient lighting products, such as LED lighting;
- setting and keeping the air conditioners to a default temperature of around 24 to 26 degrees; and
- conducting regular inspection and maintenance of vehicles and equipment.

Our total cost of compliance with environmental protection and health and safety laws and regulations in 2021 and 2022 was RMB95,000 and RMB90,000, respectively. We do not expect our costs of complying with current and future environmental protection and health and safety laws to increase significantly going forwards.

In addition to environmental protection, we have also adopted a series of measures to enhance clinical trial safety through (i) complying with relevant regulations once our drugs are approved, including but not limited to, (a) regularly checking regulatory developments and updates, (b) developing clinical trial protocols with reference to the latest regulations and guidelines on clinical trial safety and (c) communicating with relevant employees and CROs on the regulatory compliance update and the enforcement of clinical trial protocols, and (ii) establishing and enforcing internal policies and procedures on clinical trial safety, starting with (a) monitoring adverse events of drugs and drug candidates from literature, social media, reports and clinical trials as well as creating safety management plans and recording properly and accurately the clinical trial safety events for each clinical trial, (b) conducting comprehensive analysis on the collected adverse events and evaluating the safety risks, (c) reporting serious adverse events and potential serious safety risks to regulatory authorities promptly and then (d) revising protocols, investigators' brochures and informed consent forms and re-evaluating the safety risks periodically.

Furthermore, we will adopt various strategies and measures to identify, assess, manage and mitigate environmental, social and climate-related risks, including but not limited to:

- reviewing and assessing the ESG reports of similar companies in the industry to ensure that all relevant ESG-related risks are identified on a timely basis.
- discussing among management from time to time to ensure all the material ESG areas are recognized and reported.
- discussing with key stakeholders on key ESG principles and practices to ensure that the significant aspects are covered.
- organizing a specific ESG risk management process to identify and consider ESG risks and opportunities separate from other business risks and opportunities.
- setting targets for environment KPIs, including with regard to emission, pollution and other impact on the environment aimed at reducing emissions and natural resource consumption.

We will adopt comprehensive measures to mitigate environmental impact from our business, strategy and financial performance in the near, medium and long term, as summarized below:

| **Focus areas** | **Key measures** |
|---|---|
| Exhaust gas management | • Adopt exhaust gas treatment system and install active carbon filters |
| Greenhouse gas management | • Increase the use of clean energy |

| Focus areas | Key measures |
|---|---|
| | • Use energy efficient equipment |
| Sewage management | • Install sewage treatment system |
| Solid waste management | • Require proper handling and disposal of solid waste |
| | • Set up hazardous waste storage sites in accordance with relevant standards and establish standardized hazardous waste management system |
| | • Engage qualified third-party suppliers for solid waste disposal |
| Energy and resource conservation | • Improve energy-saving features such as energy-saving transformers |
| | • Conserve water by recycling rain water and installing low-flow valves |

Our Group will conduct an enterprise risk assessment at least once a year to cover the current and potential risks faced by our Group, including, but not limited to, the risks arising from the ESG aspects and strategic risk around disruptive forces such as climate change. Our Board will assess or engage an external expert to evaluate the risks and review our Group's existing strategy, target and internal controls, and necessary improvement will be implemented to mitigate the risks. Our Board, Audit Committee, and the ESG Committee will maintain oversight of our Group's approach to risk management, including climate-related risks and risks monitored as part of the standard operating processes to ensure the appropriate mitigations are in place of the regular management reviews.

The decision to mitigate, transfer, accept or control risk is influenced by various factors such as government regulation, transportation network and public perception. Our Group will incorporate climate-related issues, including physical and transition risk analysis, into our risk assessment processes and risk appetite setting. If the risk and opportunities are considered material, our Group will make reference to them in the course of the strategy and financial planning process. Upon annual review of the environmental, social and climate-related risks and our Group's performance in addressing the risks, we may revise and adjust the ESG strategies as appropriate.

## Metrics and Targets

We have monitored the following metrics to assess and manage the environmental and climate-related risks arising from our business and manufacturing operations since 2021:

***Resource Consumption***

- *Electricity consumption.* We have monitored our electricity consumption levels and implement measures to improve energy efficiency since 2021. In 2021 and 2022, our electricity consumption levels were 0.2 million kWh and 0.2 million kWh, respectively. We intend to reduce the level of our per capita electricity consumption by approximately 10% per thousand dollars of R&D expense by 2023 through (i) installing energy efficient lighting in future decoration and ensuring lights are switched off when not in use either manually or through automatic sensors, and (ii) switching off certain IT equipment or setting up automatic power shutdown for certain systems and devices when not in use.

- *Water consumption.* We have monitored our water consumption levels and implement measures to promote water conservation since 2021. In 2021 and 2022, our water consumption levels were 323 tons and 281 tons, respectively. We intend to reduce the level of our per capita water consumption by approximately 10% per thousand dollars of R&D expense by 2023 through (i) selecting, installing and maintaining water-saving devices and appliances to avoid waste, and (ii) posting slogans on saving water in our office, encouraging employees to save water in their daily life, including when working in the office.

***Discharge Management***

- *Greenhouse gas discharge.* We have monitored our GHG discharge levels on a periodic basis since 2021. In 2021 and 2022, our GHG emissions were approximately 117.86 tons and 126.43 tons, respectively. We intend to reduce the level of our per capita GHG discharge by approximately 10% per thousand dollars of R&D expense by 2023 through (i) putting forward strict environmental protection requirements in the process of selecting suppliers of raw materials and consumables, (ii) reducing the use of air conditioners in our laboratories to the extent possible, especially in winter, and (iii) limiting business air travels and replacing long-journey in-person meetings with virtual conferences where possible.

- *Hazardous waste discharge.* We have monitored our hazardous waste discharge levels on a periodic basis since 2021. In 2021 and 2022, our hazardous waste discharge levels were approximately 2.12 tons and 1.97 tons, respectively, and such waste was disposed by qualified third parties. We intend to reduce the level of our per capita hazardous waste discharge by approximately 10% per thousand dollars of R&D expense by 2023 through measures, including but not limited to, (i) regularly monitor and assess sources of hazardous waste generation and replace or optimize

processes, projects, materials and equipments that tend to unnecessarily generate such waste, such as replacing 96-well plates with 384-well plates to improve efficiency in cell proliferation experiments to reduce liquid hazardous waste produced in the process, (ii) enhance our on-site waste treatment capacities, including installing more equipment as appropriate to reduce pollutant concentration in effluent to render it non-toxic or less harmful, (iii) work with professional waste processors, such as specialized sewage treatment centers, to make hazardous waste non-toxic or less harmful, and (iv) other measures that we may find helpful in reducing our hazardous waste discharge in the future.

Our Board will set targets for each material KPIs at the beginning of each financial year in accordance with the disclosure requirements of Appendix 27 to the Listing Rules and other relevant rules and regulations upon [**REDACTED**]. The relevant targets on material KPI will be reviewed on an annual basis to ensure that they remain appropriate to the needs of our Group. In setting targets for the ESG-related KPIs, we have taken into account our respective historical consumption or discharge levels during the Track Record Period, and have considered our future business expansion in a thorough and prudent manner with a view of balancing business growth and environmental protection to achieve sustainable development.

**Workplace Safety**

We have adopted and maintained a series of rules, standard operating procedures, and measures to maintain our employees' healthy and safe environment. We implement safety guidelines to set out information about potential safety hazards and procedures for operating in the manufacturing facilities. We require new employees to participate in safety training to familiarize themselves with the relevant safety rules and procedures. In particular, we conduct training sessions on fire control safety and regularly perform emergency evacuation drills to reduce risks associated with potential fire accidents. Also, we have policies in place and have adopted relevant measures to ensure the hygiene of our work environment and the health of our employees.

We provide company-level and department-level training for all new hires so that our employees are effectively familiarized with each other's responsibilities. We provide training in systematic management theory, technology and application skills for middle and senior management. Staff in specialized departments, such as finance and R&D, receive basic training in their field and gain up-to-date business knowledge. We have established an employee performance management system that provides regular reviews of compensation and development for high-performing employees. We provide benefits such as an improved health insurance plan to bring a better welfare experience to our employees. We use equity incentives as a long-term incentive plan to encourage employees to start and grow with the company.

Our PRC Legal Adviser has confirmed that, during the Track Record Period and up to the Latest Practicable Date, we had not been subject to any material claim or penalty in relation to health, work safety, social and environmental protection, and had been in compliance with the relevant laws and regulations in China in all material aspects.

## PERMITS, LICENSES AND OTHER APPROVALS

As of the Latest Practicable Date, our PRC Legal Adviser confirmed we had obtained requisite licenses, approvals and permits from relevant Chinese authorities that are material to our operations in China, and such licenses, permits and certifications all remain in full effect. For more details regarding the laws and regulations to which we are subject, please see the section headed "Regulatory Overview" in this document. We had not experienced any material difficulty in renewing such licenses, permits, approvals and certificates during the Track Record Period and up to the Latest Practicable Date, and we currently do not expect to have any material difficulty in renewing them when they expire, if applicable. There is no material legal impediment in renewing such licenses, permits, approvals and certificates as they expire in the future as long as we are in compliance with applicable laws, regulations and rules. During the Track Record Period and up to the Latest Practicable Date, we had not been penalized by any government authorities for any material non-compliance relating to maintenance and renewal of our material licenses, permits, approvals and certificates.

## LEGAL PROCEEDINGS AND COMPLIANCE

### Legal Proceedings

During the Track Record Period and up to the Latest Practicable Date, we were not a party to any actual or threatened legal or administrative proceedings. We are committed to maintaining the standards of compliance with the laws and regulations applicable to our business. However, we may from time to time be subject to various legal or administrative claims and proceedings arising in the ordinary course of business.

### Legal Compliance

Our PRC Legal Adviser confirmed that during the Track Record Period and up to the Latest Practicable Date, we had complied with applicable laws and regulations in China in all material aspects. Our Directors confirmed that we were not involved in any material or systematic non-compliance incidents.

Our compliance team is responsible for building, developing and improving our compliance management system to ensure our compliance culture is embedded into everyday workflow. The team conducts compliance training for target groups and identifies, assesses, and reports compliance risks and expectations in a timely manner. For example, we provide formal and comprehensive company-level legal seminars to our employees, followed by on-the-job training to efficiently get them familiarized with their responsibilities and our compliance requirements. Our compliance team will also work with the senior management team to monitor and evaluate the effectiveness of our compliance function and structure to ensure that we comply with the applicable laws and regulations. For example, we will periodically conduct compliance and performance reviews on our employees against our internal compliance standards to ensure their compliance awareness meets our requirements.

## RISK MANAGEMENT AND INTERNAL CONTROL

### Risk Management

We are exposed to various risks in our business operations, and we believe that risk management is important to our success. For details, see "Risk Factors – Risks Relating to Our Operations". Our Directors oversee and manage the overall risks associated with our operations. We have prepared written terms of reference in compliance with Rule 3.21 of the Listing Rules and the Corporate Governance Code and Corporate Governance Report as set out in Appendix 14 to the Listing Rules.

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

- 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;
- provide anti-corruption and anti-bribery compliance training periodically to our senior management and employees to enhance their knowledge and compliance with applicable laws and regulations; and
- attend training sessions by our Directors and senior management in respect of the relevant requirements of the Listing Rules and duties of directors of companies [**REDACTED**] in Hong Kong.

### Internal Control

We have engaged an independent internal control consultant to assess our internal control system in connection with the [**REDACTED**]. The internal control consultant has conducted a review procedure on our internal control system in certain aspects, including financial reporting and disclosure controls, corporate level controls, information system control management and other procedures for our operations. The internal control consultant has not identified any material deficiencies in our internal system.

We have also appointed external legal counsels to advise us on compliance matters, such as compliance with the regulatory requirements on clinical research and development, which is also monitored by our regulatory and quality assurance team. We have also established anti-bribery guidelines and compliance requirements in our employee handbook. After considering the remedial actions we have taken, our Directors are of the view that our internal control system is adequate and effective for our current operations.

We plan to provide our Directors, senior management, and relevant employees with continuous training programs and updates regarding the relevant laws and regulations in China and the U.S. regularly to proactively identify any concerns and issues relating to any potential non-compliance.

***Anti-Bribery***

We maintain strict anti-corruption policies among our employees. We believe we will be less affected by the increasingly stringent measures taken by the Chinese government to correct corruptive practices in the pharmaceutical industry. We strictly prohibit bribery or other improper payments in our business operations. This prohibition applies to all business activities, anywhere globally, whether involving government officials or healthcare professionals. Improper payments prohibited by this policy include bribes, kickbacks, excessive gifts or entertainment, or any other payment made or offered to obtain an undue business advantage. We keep accurate books and records that reflect transactions and asset dispositions in reasonable detail. Requests for false invoices or payment of unusual, excessive or inadequately described expenses are rejected and promptly reported. Misleading, incomplete or false entries in our books and records are never acceptable. We will also ensure that future commercialization team personnel comply with applicable promotion and advertising requirements, including restrictions on promoting drugs for unapproved uses or patient populations and limitations on industry-sponsored scientific and educational activities.

***Data Privacy Protection***

We have established procedures to protect the confidentiality of patients' data. We maintain policies requiring our personnel to be trained to collect and safeguard personal information and require our CROs to have data protection clauses in our agreements with them. They are responsible for safeguarding data in their possession. According to the GCP and relevant regulations, access to clinical trial data has been strictly limited to authorized personnel.

Additionally, we require external parties and internal employees involved in clinical trials to comply with confidentiality requirements. Data are to be used only for the intended use, as agreed by the patients and consistent with the Informed Consent Form (the "**ICF**"). We will obtain consent from patients if any use of data falls outside the scope of ICF.

We have a number of ongoing or planned clinical studies in China and the U.S. Any transfer of clinical trial data in connection with our product development efforts and regulatory communications is subject to the applicable local data and privacy protection laws, including those in China and the U.S. Together with our CROs and other collaborators, we have implemented controls and arrangements designed to ensure a data management and transfer plan is developed and implemented to govern the transfer of all clinical trial data or other potentially sensitive information. Related measures include, as applicable, ensuring that the cross-border transfer of this clinical data and information is permitted, any requisite approvals are properly obtained, and applicable filings are made, in each case, with the competent authorities and in accordance with relevant laws and regulations (particularly in the case of any transfer between China and the U.S.). Although the laws and regulations in this area and the nature of our potential clinical studies are evolving, to date, we have not experienced any material difficulty in data transfer, and we believe our transfer of relevant clinical trial data and information between China and the U.S. is in line with market practice.