*The information and statistics set out in this section and other sections of this document were extracted from different official government publications, available sources from public market research and other sources from independent suppliers, and from the independent industry report prepared by China Insights Consultancy (the "**CIC Report**"). We engaged China Insights Consultancy, an independent industry report, to prepare the CIC Report in connection with the* [**REDACTED**]. *The information from official government sources has not been independently verified by us, the Sole Sponsor, the* [**REDACTED**], *[the* [**REDACTED**], *the* [**REDACTED**], *the* [**REDACTED**] *and the* [**REDACTED**]*], any of the* [**REDACTED**], *any of their respective directors and advisers, or any other persons or parties involved in the* [**REDACTED**] *(other than CIC), and no representation is given as to its accuracy.*

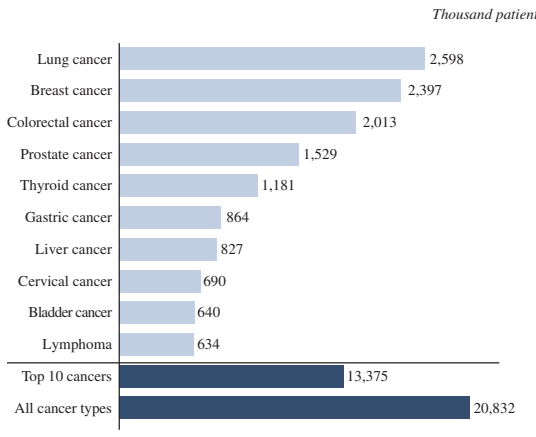
THE CANCER TREATMENT MARKET

Cancer is a broad group of diseases in which abnormal cells grow in an uncontrolled manner and spread locally or to distant parts of the body. It is the leading cause of mortality worldwide with 10 million deaths globally and over 2.5 million deaths in China in 2024. Global cancer incidence reached 20.8 million in 2024 and is expected to reach 26.6 million in 2035. In China, cancer incidence was 5.1 million in 2024 and is expected to reach 6.3 million in 2035.

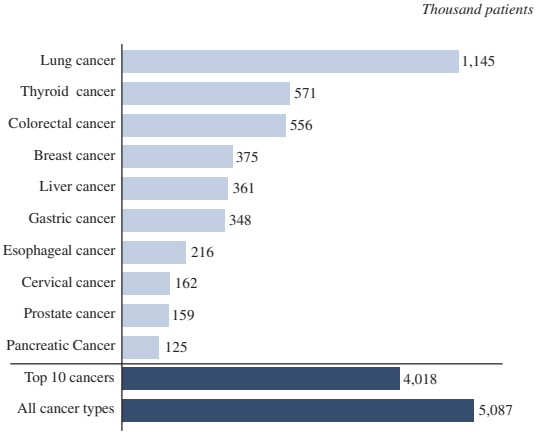
Cancer Epidemiology

As illustrated in the charts below, China has an overlapping but different profile of top ten cancers by incidence compared to that globally, with lung cancer, CRC and thyroid cancer being the most common cancer types. Despite the differences in ranking, several cancer types are among the top ten cancers by incidence both globally and in China, including BC and GC, indicating vast addressable patient populations for these cancer types both globally and in China.

Cancer incidence around the globe, 2024



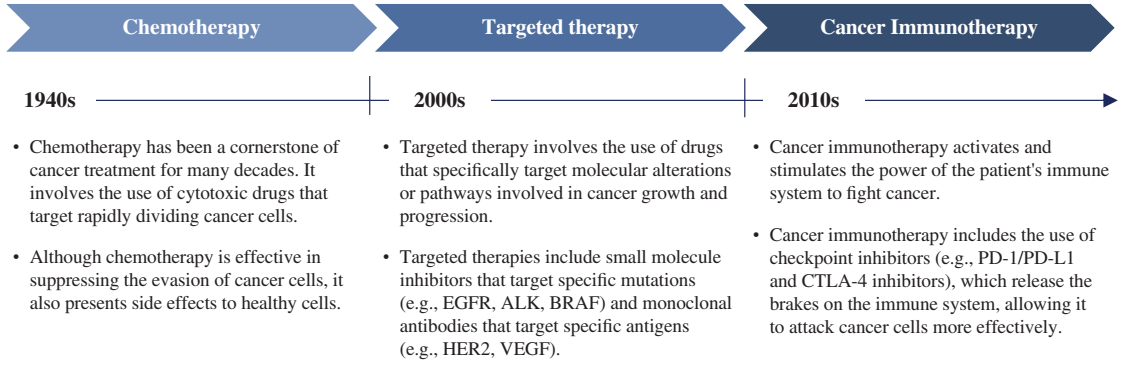
Cancer incidence in China, 2024



Source: National Central Cancer Registry of China (NCCR), World Health Organization (WHO), CIC

Evolution of Cancer Drugs

Cancer drugs have evolved rapidly over the past few decades. As illustrated in the diagram below, the landscape of cancer drugs has progressed from chemotherapy to targeted therapy using small molecule inhibitors that target specific mutations and mAbs that target specific antigen. It has then advanced to immunotherapy, which activates and stimulates the patient's own immune system to fight cancer.



Cancer immunotherapy is a revolutionary cancer treatment which aims to fight tumor cells through the stimulation and activation of patients' own immune systems. Compared with traditional cancer treatments, immunotherapy generally presents a better safety profile with lower impact on healthy cells, wider indication coverage by using targets overexpressed across different types of cancers, and better efficacy by harnessing the power of immune systems. Patients treated with immunotherapy may experience durable responses where the immune system continues to recognize and attack cancer cells, potentially leading to sustained anti-tumor activity. In addition, immunotherapy can be combined with traditional treatments to further enhance treatment outcomes through synergistic effects.

Market Size

The global and China's cancer treatment markets have expanded rapidly in recent years. The global cancer drug market grew from US$129.0 billion in 2018 to US$262.1 billion in 2024 at a CAGR of 12.5% and is expected to reach US$600.6 billion in 2035 at a CAGR of 7.8% from 2024. The cancer drug market in China increased from RMB143.0 billion in 2018 to RMB267.6 billion in 2024 at a CAGR of 11.0% and is projected to continue its robust growth, reaching RMB795.8 billion in 2035 at a CAGR of 10.4% from 2024.

THE CANCER IMMUNOTHERAPY MARKET

Cancer immunotherapy is a novel treatment modality that harnesses the patient's own immune system to generate or amplify anti-tumor immune responses, thereby enabling the body to effectively recognize and eliminate malignant cells.

Market Size

The cancer immunotherapy market represents the market for antibody-based cancer immunotherapy drugs, including ICIs, T cell engagers and other antibody-based modulators. The global and China's cancer immunotherapy markets have expanded rapidly in recent years. The global cancer immunotherapy market rose from US$18.6 billion in 2018 to US$62.8 billion in 2024 at a CAGR of 22.5% and is expected to reach US$266.1 billion in 2035 at a CAGR of 14.0% from 2024. The cancer immunotherapy market in China grew from RMB0.8 billion in 2018 to RMB24.4 billion in 2024 at a CAGR of 77.2% and is forecasted to continue its strong growth, reaching RMB272.4 billion in 2035 at a CAGR of 24.5% from 2024.

Antibody-based immunotherapies are designed to engage specific molecular targets involved in disease pathogenesis and immune systems. Within this category, ICIs have emerged as a promising approach for their remarkable efficacy in treating various types of malignancies and their potential to revolutionize the landscape of cancer treatment, making it a dominant category in the current cancer immunotherapy landscape. As of December 31, 2025, over 30 ICIs have been approved globally, most of which are monoclonal antibodies that target the three validated targets, namely PD-1, PD-L1 and CTLA-4. ICIs represented a breakthrough in cancer treatment in recent years and the indications for ICIs continue to expand.

While global annual sales of PD-(L)1-targeting inhibitors have reached over US$59.9 billion in 2024, approved ICIs have significant limitations. The ORR of ICI treatment is limited. According to an analysis encompassing 91 clinical trials with a total of 16,400 patients, the mean ORR for PD-(L)1 inhibitors was less than 20%. Resistance to ICIs can arise due to the complex and dynamic nature of the interactions between the immune system and the TME. Cancer cells are constantly evolving and adapting to survive under the selective pressure of the immune response, highlighting the need for further advancements in this field to improve patient outcomes.

Market Drivers

The unmet needs of a large patient population, as well as new therapeutic strategies that are being explored to address these needs, is expected to drive the growth of cancer immunotherapy market. Specifically, the growth of the cancer immunotherapy market is driven primarily by the following factors:

Expanding Patient Base with Significant Unmet Needs. The aging population and lifestyle factors have substantially contributed to an increased cancer patient pool, which has in turn driven the expansion of the cancer therapy market globally and in China. The five-year survival rate for many major cancer types including lung cancer and GC is lower than 35%, calling for therapies with better efficacy. Although immunotherapy such as ICIs have brought novel treatment options to patients, the ORR is still unsatisfactory. Among the most common cancer types, the ORR is 26.9% for lung cancer and is even lower for HNC and GC at only approximately 12%. Drug resistance and risks of serious side effects, as well as limited effective treatment options available to late-line patients, indicate significant unmet needs for more innovative therapies to improve cancer prognosis and outcome.

Growing Understanding of Tumor Microenvironment. The TME has emerged as a critical player in cancer progression, metastasis, and response to therapies. Growing evidence suggests that the effectiveness of ICIs depends largely on the condition of the TME. "Cold" tumors, characterized by either a lack of infiltrating T cells or the existing T cells being functionally suppressed by the presence of various inhibitory factors in the TME, are generally less responsive to ICIs. Due to the high complexity of the TME and the interactions of multiple signaling pathways, conventional monoclonal ICIs struggle to achieve satisfactory clinical response rates and durable efficacy. Strategies to change the TME, including by reinvigorating T cells and removing immunosuppressive factors within the TME, are being explored. Among the major components of TME, TAMs have gained increasing attention as potential therapeutic targets. There is a growing trend of employing advanced technologies to unravel the heterogeneity of TAMs across different tumor types, stages, and locations, paving the way for innovative therapies.

Innovative Targets and Mechanisms of Action. Deepening insights of cancer biology has fueled the growing recognition of the need for innovative therapies that target multiple biomarkers or mechanisms. Together with an enhanced understanding of the role of immune system in cancer progression, the use of agents with new targets or mechanisms of action will drive the development of novel strategies, leading to better patient outcomes and a paradigm shift in cancer treatment.

Advancement in Antibody Drug Development Platform and Emergence of New Modalities. Significant advancements in antibody drug development platforms in recent years allow for the rapid development of novel treatment modality, including bsAbs. Compared to mAbs, bsAbs are expected to have improved clinical benefits by simultaneously binding to two different antigens. These new modalities serve as powerful tools for generating novel therapies that can target specific cancer antigens, overcome drug resistance, and improve patient outcomes. As these platforms and modalities continue to evolve, they are expected to play a crucial role in driving innovation in cancer treatment and satisfying the ever-changing landscape of unmet medical needs.

Increasing Use of Combination Therapy. Combination therapy, which involves the use of multiple agents with distinct mechanisms, has become increasingly common. By targeting different pathways or immune checkpoints, combination therapy can generate synergistic effects, overcome resistance mechanisms, and improve treatment outcomes. The development of novel treatment modalities is also expected to result in a greater number and variety of combination treatments.

Entry Barriers

There are a number of ongoing challenges in the development of cancer immunotherapy. Primary entry barriers of the cancer immunotherapy market are set forth as follows.

R&D capabilities and accumulated expertise. Development of cancer immunotherapy requires strong research capabilities, accumulated expertise, and integration of knowledge from multiple disciplines and special skill sets. The lack of tumor-specific antigens identified and the potential of off-target toxicities due to shared antigen expression between healthy tissues and cancer cells also complicate the selection of targets with efficacy and safety. In addition, development of cancer immunotherapy requires a deep understanding of the interactions between tumor cells, immune cells, and the multiple pathways involved in immune response, which in turn requires the understanding of TME. Moreover, selecting the desired molecule structures that link the intended mechanisms of actions with clinical applications require extensive engineering experience.

Complex development process. Translating preclinical findings into successful clinical outcomes is a major hurdle in the development of cancer immunotherapy. Drug candidates may also cause AEs and undesirable side effects, among other unexpected characteristics, which could result in a suspension or termination of an ongoing trial. As such, the process of developing immunotherapy and obtaining regulatory approval can be more time-consuming and requires heavy capital investment, making it a challenge for new entrants and players to the cancer immunotherapy market.

Stringent and evolving regulation. The approval for cancer immunotherapy involves a complex registration and approval process. In addition, the regulatory environment for the development, commercialization, registration and post-approval monitoring of cancer drugs has been constantly evolving in recent years. These stringent and evolving regulatory challenges and considerations create a high entry barrier to the cancer immunotherapy market.

CHINA'S OX40 AGONIST MARKET

Overview

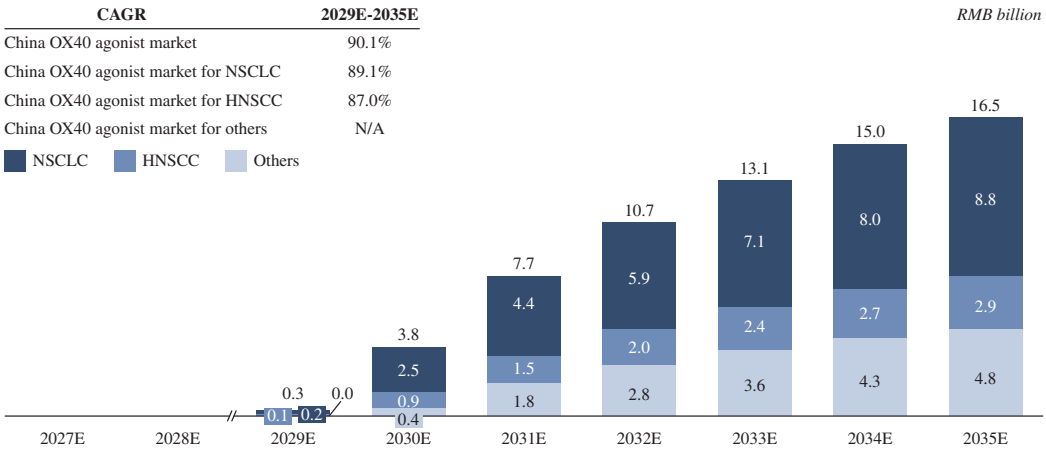
OX40, also known as CD134, is a validated co-stimulatory receptor that is predominantly expressed on activated T cells. OX40 signaling improves T cell immunity function by contributing to the expression of pro-survival molecules, elevating cytokine production and augmenting the generation of both effector and memory T cell subsets. OX40 agonists can further augment OX40 signaling, therefore increasing T cell infiltration into tumors and enhancing T cell-mediated anti-tumor immune responses.

Due to the ability of OX40 signaling to enhance anti-tumor immunity, there have been many efforts to exploit this pathway for immunotherapy targeting various types of cancers. As of the Latest Practicable Date, there were no approved OX40 agonists across the globe and in China. Most OX40 agonists under development are bivalent, having two binding sites that can attach to the OX40 receptor on immune cells. This bivalent configuration is poorly suited for efficient receptor clustering, a fundamental process in cell signaling that involves the aggregation of cell surface receptors, as demonstrated by the unsatisfactory clinical responses observed for such molecules. OX40 agonists engineered with a hexavalent configuration have shown encouraging early data in eliciting superior anti-tumor activity compared to bivalent OX40 agonists given the trimeric nature of OX40L, the ligand of OX40, to achieve improved receptor clustering and downstream signaling.

Addressable Market Size

The first OX40 agonist in China is expected to be approved by 2029 and China's OX40 agonist market is expected to reach RMB16.5 billion by 2035, growing at a CAGR of 99.6% from 2029. The following charts set forth the addressable market size of OX40 agonist in China.

Market size of China OX40 agonist, 2026E-2035E



Source: WHO, IARC, CIC

Approximately 15-20% of the NSCLC patients in China can potentially be treated by the OX40 agonists currently under clinical development after they obtain regulatory approval, according to CIC. The incidence of NSCLC cases in China that can potentially be treated by OX40 agonists is expected to increase from 166.7 thousand in 2024 to 190.2 thousand in 2028 with a CAGR of 3.3%, and is expected to reach 226.6 thousand cases in 2035 with a CAGR of 2.5% from 2028. Approximately 40-50% of HNSCC patients in China can potentially be treated by the OX40 agonists currently under development after they obtain regulatory approval, according to CIC. The incidence of HNSCC cases in China that can potentially be treated by OX40 agonists is expected to increase from 64.4 thousand in 2024 to 68.9 thousand in 2028 with a CAGR of 1.7%, and is expected to reach 75.6 thousand cases in 2035 with a CAGR of 1.4% from 2028.

Competitive Landscape

As of the Latest Practicable Date, there were no approved OX40 agonists worldwide and ES102 was one of the only two OX40 agonist candidates in phase 2 or beyond under clinical development in China. Of these candidates, a number are being developed as a combination therapy with chemotherapy or mAbs. In China, there were eight OX40 agonist candidates in clinical development as of the Latest Practicable Date. As of the same date, there were eleven OX40 agonist

candidates in clinical development outside China, with potential for future entry into the Chinese market upon regulatory approval. A summary of the competitive landscape of OX40 agonists in China as of the Latest Practicable Date is set forth below.

Competitive landscape of OX40 agonists in China

Candidate	MoA	Configuration	Company	Clinical Phase	Indication	Mono/Combo	First Post Date
ES102	**OX40 mAb**	**Hexavalent**	**Our Group**	**2**	**Advanced NSCLC**	**Combo**	**2024/01/29**
				1	**Advanced Solid Tumors, including NSCLC and HNSCC**	**Combo**	**2021/08/05**
				1	**Advanced Solid Tumors, including NSCLC**	**Mono**	**2021/07/09**
BGB-A445	OX40 mAb	Bivalent	BeiGene	2	NSCLC	Combo	2023/09/27
				2	Advanced NSCLC	Combo	2023/03/29
HX111	OX40 ADC	N/A	Hanx Biopharmaceuticals	1/2a	Advanced Solid Tumors and Hematologic Malignancies	Mono	2025/12/24
IBI101	OX40 mAb	Bivalent	Innovent Biologics	1a/1b	Advanced or Metastatic Solid Tumors	Mono & Combo	2018/10/19
HLX51	OX40 mAb	Tetravalent	Henlius Biotech	1	Advanced Solid Tumors	Mono	2023/06/27
YH002	OX40 mAb	N/A	Eucure Biopharma	1	Advanced Solid Tumors	Combo	2022/04/28
BAT-6026	OX40 mAb	Bivalent	Bio-Thera Solutions	1	Advanced or Metastatic Solid Tumors	Mono	2021/09/27
ABBV-368	OX40 mAb	Bivalent	AbbVie	1	Advanced or Metastatic Solid Tumors, including TNBC and NSCLC	Combo	2019/05/27

Source: CDE, CIC

NSCLC

Lung cancer is the most common cancer worldwide and in China. In China, the incidence of lung cancer increased from 899.3 thousand cases in 2018 to 1,144.9 thousand cases in 2024 and is expected to reach 1,556.2 thousand cases in 2035. NSCLC is the most common subtype of lung cancer, representing approximately 85% of all lung cancer types globally, and a leading cause of cancer death with unmet medical need in China. Approximately 15-20% of the NSCLC patients in China can potentially be treated by the OX40 agonists currently under clinical development after they obtain regulatory approval, according to CIC. The incidence of NSCLC cases in China that can potentially be treated by OX40 agonists is expected to increase from 166.7 thousand in 2024 to 190.2 thousand in 2028 with a CAGR of 3.3%, and is expected to reach 226.6 thousand cases in 2035 with a CAGR of 2.5% from 2028.

Treatment Paradigm

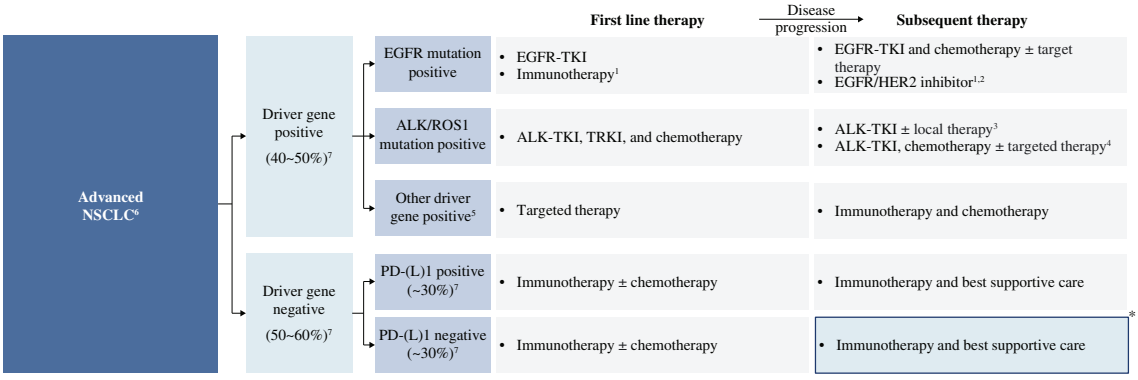
NSCLC is the most common subtype of lung cancer, representing approximately 85% of all lung cancer types globally. NSCLC can be broadly classified as early-stage NSCLC and advanced NSCLC. Early-stage NSCLC patients represent patients with localized early tumors, which account for approximately 30-40% of total NSCLC incidence. In China and the U.S., for early-stage NSCLC patients, surgery is the primary treatment option. For patients whose conditions are not suitable for surgery, chemotherapy and radiotherapy are recommended.

Advanced NSCLC patients represent patients with locally advanced or metastatic tumors, which account for approximately 60-70% of total NSCLC incidence. The treatment paradigm of advanced NSCLC can be broadly classified based on molecular testing and PD-L1 testing results. For advanced NSCLC patients with positive oncogenic drivers, which are genetic mutations or alterations that contribute to the development and progression of cancers, targeted therapy is the standard of care for patients. For advanced NSCLC patients with negative oncogenic drivers, immunotherapy such as use of ICIs and chemotherapy are commonly used. However, among the NSCLC patients with negative oncogenic drivers, only a limited percentage of patients are

responsive to PD-(L)1 regimen. Additionally, a global retrospective multicenter registry IMMUNOTARGET has demonstrated that anti–PD-(L)1 agents as monotherapy have, in general, low response rates in the treatment of NSCLC patients, due to the lack of CD8+ TILs characteristic of "cold" tumors.

Among advanced NSCLC patients, apart from the about 40-50% of patients who are potentially eligible for targeted therapies and the approximately 30% who exhibit high expression of PD-(L)1, approximately 30% do not respond to existing therapies, which indicates unmet medical needs. This group of patients, which accounts for approximately 15-20% of the total NSCLC population, can potentially be treated by OX40 agonists.

The table below illustrates the treatment paradigm for advanced NSCLC in China.



Notes:

1. If EGFR ex20ins mutation positive; 2. EGFR/HER2 inhibitor = sunvozertinib; 3. Treatment for oligoprogress/central nervous system (CNS) metastasis; 4. Switch to alternative ALK-TKI, if progress on all TKIs, platinum-based chemotherapy ± VEGF targeted therapy; 5. For KRAS G12C and HER-2 positive patients, refer to driver gene negative first line/subsequent treatment; 6. Early-stage NSCLC = NSCLC patients with localized early tumor. Advanced NSCLC = locally advanced and metastatic NSCLC; 7. Percentage represents ratio of number of selected patient group to total advanced NSCLC, which accounts for 60~70% of total NSCLC incidence

* The highlighted column indicates the patient group of ES102. ES102, developed by our Group, targets advanced NSCLC patients who are refractory or resistant to immunotherapies and is undergoing a phase 2 clinical trial in combination with toripalimab as 2L or 3L treatment for patients with advanced NSCLC in China.

Source: CSCO, CIC

HNSCC

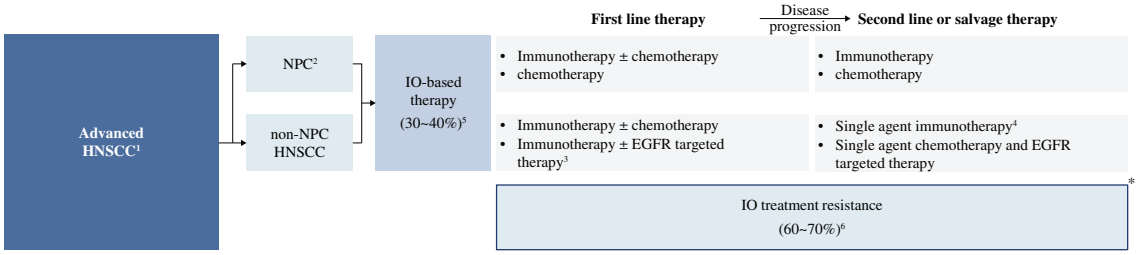
HNSCC is a group of cancers arising from mucosal surfaces of the mouth, nose and throat and accounts for approximately 90% of HNC. In China, the incidence of HNC increased from 134.8 thousand cases in 2018 to 151.2 thousand in 2024 and is expected to reach 177.6 thousand cases in 2035. Approximately 40-50% of HNSCC patients in China can potentially be treated by the OX40 agonists currently under development after they obtain regulatory approval, according to CIC. The incidence of HNSCC cases in China that can potentially be treated by OX40 agonists is expected to increase from 64.4 thousand in 2024 to 68.9 thousand in 2028 with a CAGR of 1.7%, and is expected to reach 75.6 thousand cases in 2035 with a CAGR of 1.4% from 2028.

Treatment Paradigm

In China, for early-stage HNSCC patients, surgery and radiotherapy are the primary treatment options. Advanced HNSCC, which includes locally advanced and/or neck recurrent HNSCC and metastatic HNSCC, accounts for approximately 70% of total HNSCC incidence. For advanced HNSCC patients, although immunotherapy such as nivolumab with or without chemotherapy is recommended, the ORR of ICIs like nivolumab in the total advanced HNSCC patient is

approximately 36%, indicating that around 60% of advanced patients exhibit primary resistance and do not respond to ICI treatments. This group of patients, which accounts for approximately 40-50% of the total HNSCC population, can potentially be treated by OX40 agonists. Consequently, there is a pressing need for therapies such as OX40 agonists that can achieve higher response rates and enhance overall survival in advanced HNSCC patients.

The table below illustrates the treatment paradigm for advanced HNSCC in China.



Notes:

1. Advanced HNSCC = locally advanced and/or neck recurrent HNSCC and metastatic HNSCC; 2. Nasopharyngeal cancer; 3. EGFR targeted therapy = cetuximab; 4. Single agent immunotherapy = nivolumab, GRADE I recommendation; 5. Percentage represents ratio of number of selected patient group that respond to immunotherapy to total advanced HNSCC, which accounts for approximately 70% of HNSCC incidence; 6. Percentage represents ratio of number of selected patient group that do not respond to immunotherapy to total advanced HNSCC, which accounts for approximately 70% of HNSCC incidence

* The highlighted column indicates the targeted patient group of ES102. ES102, developed by our Group, targets locally advanced recurrent or metastatic HNSCC and is undergoing clinical development potentially as early-line treatments in combination with ICIs such as PD-(L)1 antibodies for patients with advanced HNSCC in China.

Source: CSCO, CIC

GLOBAL AND CHINA'S CD39/TGFβ BSAB MARKET

Overview

A majority of cancers fail to respond to immunotherapy with ICIs due to high levels of adenosine and TGFß in the TME. The CD39 pathway is considered to be one of the major sources of adenosine in the TME by mediating dephosphorylation of ATP to ADP and AMP. CD39 is widely expressed in various cancer TMEs, including NSCLC, ESCC, GIST and desmoid tumor. Antibodies that bind to CD39 can prevent ATP processing, which in turn prevents adenosine-mediated immune suppression and enhances T-cell activation. TGFß is a cytokine that is expressed at elevated levels in late-stage primary and metastatic tumors. Nearly every cell in TME responds to TGFβ, and such diverse biological responses have a variety of effects on tumor progression. For example, TGFß enables tumors to evade immune surveillance, induces the differentiation of Tregs, which, in turn, inhibits inflammation through the production of immune suppressive cytokines. TGFß also induces the expression of inhibitory molecules, such as CTLA-4 and CD39.

The dual-inhibition of the CD39-adenosine pathway and the TGFß pathway can potentially overcome resistance to existing ICI therapies by counteracting TGF-mediated differentiation of Tregs and adenosine-induced immune tolerance, while protecting T cells from cell death. By fusing the extracellular structural domain of the TGFβ receptor to an antibody targeting CD39, a favorable TME can be created that inhibits adenosine formation and neutralizes the immunosuppressive effect of TGFβ.

Addressable Market Size

The first CD39/TGFβ bsAb is expected to be approved by 2029 globally and in China. The global CD39/TGFβ bsAb market is expected to reach US$10.1 billion in 2035, growing at a CAGR of 86.8% from 2029. The CD39/TGFβ bsAb market in China is expected to reach RMB10.3 billion by 2035 growing at a CAGR of 93.7% from 2029.

Competitive Landscape

As of the Latest Practicable Date, there was no approved CD39/TGFß bsAb worldwide. Other than ES014 being developed by the Group, there was no CD39/TGFß bsAb under clinical development globally. ES014 is under phase 2 clinical trials as a monotherapy with target indications of advanced solid tumors.

NSCLC

The global incidence of lung cancer increased from 2,093.9 thousand cases in 2018 to 2,598.2 thousand cases in 2024 and is expected to reach 3,431.1 thousand cases in 2035. For further details of NSCLC and its treatment paradigm, see "— China's OX40 Agonist Market — NSCLC."

ESCC

ESCC is the predominant subtype of EC, accounting for 86.3% of all EC cases in China. Global incidence of EC was 0.4 million cases in 2024 and is expected to reach 0.7 million cases in 2035. In China, annual incidence of EC was 215.9 thousand cases in 2024 and is expected to reach 186.3 thousand in 2035.

Treatment Paradigm

In the U.S., for unresectable and recurrent locally advanced ESCC patient, 1L treatment options include fluoropyrimidine plus oxaliplatin or cisplatin, with or without PD-(L)1 inhibitors nivolumab or pembrolizumab. 2L treatment options are designed based on prior therapy and performance status. Preferred regimens include use of PD-(L)1 inhibitors as monotherapy, and chemotherapy of docetaxel, paclitaxel, irinotecan and other agents.

In China, for metastatic ESCC patients, ICIs are recommended for both 1L and 2L treatment. For locally recurrent ESCC patients, if the tumor is resectable, surgery is recommended as 1L treatment. Concurrent chemotherapy plus systemic drug therapy (including ICIs) and radiotherapy is recommended as 2L treatment.

Prognosis is poor due to the limited knowledge of pathology and genetic drivers for ESCC resulting from its high mutational load. Despite the widespread use of ICIs such as PD-(L)1 in immunotherapy for ESCC, benefits provided are limited. For example, the combination of pembrolizumab and chemotherapy merely increased the modified PFS to 6.3 months from 5.8 months of chemotherapy alone.

GIST

GIST is a hard-to-treat gastrointestinal cancer with over half of advanced patients developing resistance to standard-of-care TKI-based treatments, creating demand for novel therapies targeting alternative pathways. The global incidence of GIST was 121.6 thousand cases in 2024 and is expected to reach 133.3 thousand cases in 2035. In China, the incidence of GIST was 22.9 thousand cases in 2024 and is expected to reach 24.7 thousand cases in 2035.

Treatment Paradigm

According to CSCO guidelines, the treatment of GIST is based on resectability and genotyping. For GIST patients, if the tumor is resectable, tumors below 2 cm are generally monitored through regular observation, while larger tumors are treated by surgical resection. Adjuvant therapy with imatinib is recommended only for patients assessed to be at intermediate or high risk of recurrence. For patients with advanced unresectable or metastatic or recurrent disease, imatinib is recommended as 1L treatment. A standard daily dose of 400 mg is used for patients without KIT exon 9 or PDGFRA D842V mutations, while a 600 mg daily dose is recommended for those with KIT exon 9 mutations. For patients with PDGFRA D842V mutations, avapritinib is recommended. 2L treatment options include sunitinib, ripretinib and increased-dose imatinib. Preferred subsequent therapy includes regorafenib as 3L treatment, and ripretinib as 4L treatment.

Desmoid Tumor

Desmoid tumor is a rare, locally aggressive soft tissue tumor that can cause severe pain, functional impairment, and life-threatening complications. Current treatments often lead to recurrence or significant side effects, highlighting the urgent need for more effective and safer therapies. The global incidence of desmoid tumor was 19.8 thousand cases in 2024 and is expected to reach 27.5 thousand cases in 2035. In China, the incidence of desmoid tumor was 3.6 thousand cases in 2024 and is expected to reach 4.9 thousand cases in 2035.

Treatment Paradigm

The timing of intervention is crucial for the management and treatment of desmoid tumor patients. For patients with primary or recurrent desmoid tumor, 1L management includes active monitoring for one or two years. Treatment is initiated only when there is clear clinical evidence of disease progression, typically after two or more documented progressions, and clinically appropriate. Treatment strategies vary according to tumor location. Surgical resection is preferred for desmoid tumors of the abdominal wall when feasible. In cases where surgery is not possible or results in treatment failure, systemic therapy is indicated. For desmoid tumors at other sites, systemic treatment is recommended. Neither the Desmoid Tumor Working Group nor the NCCN guidelines recommend a specific sequence or drug therapy. Commonly used targeted agents include imatinib, sorafenib and pazopanib, while chemotherapy options typically include methotrexate combined with vincristine/vinorelbine or anthracycline-based regimens.

OGSIVEO® (nirogacestat) became the first and only FDA-approved medicine for adults with desmoid tumours and was successfully launched in the U.S. in 2023. Net sales grew from US$5.4 million in Q4 2023 to US$61.5 million in Q4 2024, delivering US$172 million in the first full commercial year. The rapid uptake reflects substantial pent-up demand in an underserved patient population. Although OGSIVEO® provides demonstrable clinical benefit, treatment is accompanied by a high incidence of diarrhea (84% vs 35% placebo) and ovarian toxicity (75% vs 0% placebo in women). These safety limitations underscore the need for next-generation agents that deliver improved efficacy alongside a more favorable safety and tolerability profile.

CHINA'S VEGF/DLL4 BSAB MARKET

Overview

VEGF is an angiogenic factor that contributes to the formation of new blood vessels to support tumor cell survival and growth. VEGF signaling pathway plays an irreplaceable role in the whole process of angiogenesis of tumor issues.

DLL4, a Notch ligand, is the downstream gene of VEGF and is highly expressed in solid tumors. DLL4 plays an important role in vascular development of tumors and promotes proliferation of cancer stem cells, thereby driving the growth of malignant tumors. Blocking the

DLL4 signaling pathway can inhibit tumor progression through anti-angiogenic effect and reduction of cancer stem cells. Treatments targeting DLL4 have a significant inhibitory effect on tumor development, while have limited side effects on normal tissues.

Tumors use multiple pathways to recruit vessels and may also switch from one mechanism to another, thus blocking VEGF alone has incomplete effects on the tumor vasculature. Recent studies have shown that the use of VEGF inhibitors alone may result in a more invasive pattern of tumor development. Inherent or acquired resistance to anti-VEGF molecules may occur, leading to a lack of response and disease recurrence. Studies have also shown that some tumors naturally resistant to anti-VEGF therapy have good sensitivity to DLL4 inhibitors, and the combined use of VEGF inhibitors and DLL4 inhibitors may offer even better tumor suppressive effects. Therefore, dual blockade of the VEGF and DLL4 signaling pathways by an anti-VEGF/DLL4 bsAb has the potential to overcome resistance to anti-VEGF therapies and can be a promising therapeutic option.

Addressable Market Size

The first VEGF/DLL4 bsAb is expected to be approved by 2029 in China. The VEGF/DLL4 bsAb market in China is expected to reach RMB11.0 billion by 2035, growing at a CAGR of 119.7% from 2029.

Competitive Landscape

The FDA approved the first anti-angiogenic drug, bevacizumab (Avastin), a humanized anti-VEGF mAb, in 2004 for the treatment of previously untreated mCRC in combination with chemotherapy.

As of the Latest Practicable Date, there were no approved VEGF/DLL4 bsAbs worldwide. Other than ES104 being developed by the Group, there was no VEGF/DLL4 bsAb undergoing clinical development in China as of the same date. ES104 is under phase 1/2 clinical trials as a monotherapy in heavily pre-treated patients with advanced CRC in China.

CRC

CRC is the second most prevalent cancer in China, with annual incidence of 556.4 thousand cases in 2024, which is expected to reach 746.4 thousand cases by 2035. As CRC patients typically do not display symptoms until advanced disease, CRC is also one of the leading causes of cancer deaths in China.

Treatment Paradigm

In China, for MSS or pMMR advanced CRC patients, 1L treatment options include (i) doublet chemotherapy 5-fluorouracil/leucovorin plus either oxaliplatin ("**FOLFOX**") or irinotecan ("**FOLFIRI**") with or without cetuximab, (ii) doublet chemotherapy capecitabine plus oxaliplatin ("**CAPEOX**"), or FOLFOX or FOLFIRI with or without bevacizumab, and (iii) doublet chemotherapy fluorouracil with or without bevacizumab. In the U.S., in addition to the above treatment options, doublet chemotherapy 5-fluorouracil/leucovorin plus oxaliplatin and irinotecan ("**FOLFIRINOX**") with or without bevacizumab is also used as 1L treatment. For patients who cannot withstand higher treatment toxicity, chemotherapy 5-fluorouracil with or without bevacizumab, or capecitabine with or without bevacizumab, is recommended as 1L treatment. For patients who received oxaliplatin without irinotecan in 1L treatment, FOLFIRI with or without bevacizumab or ziv-aflibercept or ramucirumab is recommended as 2L treatment. For patients who received oxaliplatin and irinotecan in 1L treatment, 2L treatment options include (i) cetuximab or panitumumab with or without irinotecan if with wild-type KRAS/NRAS/BRAF, and (ii) biomarker-directed therapy. For patients who received irinotecan without oxaliplatin in 1L treatment, 2L treatment options include (i) FOLFOX or CAPEOX with or without bevacizumab, and (ii) targeted therapy.

VEGF plays an important role in CRC biology. Although bevacizumab has been increasingly used in 1L and 2L treatments, during bevacizumab exposure, drug resistance usually occurs, which can be demonstrated by disease progression observed in about 90% of patients within 3-12 months. In recent years, immunotherapy, including CTLA-4 and PD-(L)1 ICIs, has enriched the therapeutic modalities of CRCs. Currently, pembrolizumab and nivolumab with or without ipilimumab are approved for the treatment of patients with dMMR/MSI-H mCRC. However, only about 5% of mCRC are dMMR/MSI-H, and the remaining about 95% of mCRC patients are pMMR/MSS, which are not sensitive to ICIs, leaving a significant need for novel therapeutic options.

BTC

BTC is a primary malignant tumor of the hepatobiliary system. BTC is usually divided into gallbladder cancer, which accounted for 80% to 95% of BTC cases, and cholangiocarcinoma. In 2024, incidence of BTC was 98.3 thousand cases in China.

Treatment Paradigm

Only 20% of BTC patients are diagnosed at an early stage with a potentially resectable disease, 80% of patients do not qualify for surgical treatment. For advanced or metastatic BTC, current identified targeted therapies cover only six mutant subtypes of BTC with very limited incidence rate. The majority of mutation-negative patients still lack targeted therapies that confer long-term survival benefits.

Immunotherapy has made significant strides and its position as a mainstream treatment choice for advanced/metastatic BTC is promising. In China, durvalumab or pembrolizumab plus gemcitabine and cisplatin are recommended as 1L treatments. Preferred subsequent therapy is FOLFOX7. Other recommended 1L treatments include (i) gemcitabine plus cisplatin (category 6) or oxaliplatin or albumin-bound paclitaxel or capecitabine oxaliplatin, (ii) FOLFOX and (iii) single agents of 5-fluorouracil, capecitabine and gemcitabine. In certain circumstances, other targeted therapies are also useful. For example, for NTRK gene fusion-positive tumors, TRK inhibitors such as entrectinib and Larotrectinib are also recommended. For RET gene fusion-positive tumors, targeted therapies of pralsetinib and selpercatinib are effective.

Even though the overall survival has been significantly improved through current 1L treatment options, the ORR of immunotherapy combined with chemotherapy remains low. The ORR of BTC patients treated with ICI combined with chemotherapy is 29% compared with 29% of placebo with chemotherapy, showing no significant difference. Therefore, there is an urgent need for innovative treatment options to enhance the current BTC treatment landscape.

GLOBAL AND CHINA'S LILRB2 ANTIBODY MARKET

Overview

LILRB2 is an inhibitory receptor predominantly expressed on myeloid cells that elicits profound immune suppression. Activation of LILRB2 can trigger signals that interfere with LILRA-induced activation of multiple key immune cell responses. Interaction of LILRB2 with ligands expressed on tumor cells, including HLA-G and MHC class I molecules, results in the secretion of inhibitory factors such as TGFß, thereby promoting tumor immune evasion. LILRB2 blockade regulates cancer development by reprograming TAMs into a proinflammatory phenotype, suppressing Treg infiltration, and promoting the efficacy of an ICI. Notably, LILRB2 has one of the highest overexpression rates in OC and CRC, the lead indications of ES009.

Addressable Market Size

The first LILRB2 antibody is expected to be approved by 2029 globally and in China. The global LILRB2 antibody market is expected to reach US$6.4 billion by 2035, growing at a CAGR of 70.6% from 2029. The LILRB2 antibody market in China is expected to reach RMB6.3 billion by 2035, growing at a CAGR of 77.6% from 2029. The following charts set forth the addressable market size of LILRB2 antibody in China.

Competitive Landscape

As of the Latest Practicable Date, there were no approved LILRB2 antibodies globally. There were 13 LILRB2 antibody candidates under clinical development as of the same date, all of which were in phase 2 or earlier stages. A summary of the global competitive landscape of LILRB2 antibodies is set forth below.

Global competitive landscape of LILRB2 antibodies

Candidate	MoA	Company	Clinical Phase	Indication	Mono/Combo	Trial location
MK-4830	LILRB2 mAb	Merck Sharp & Dohme LLC	2	NSCLC, SCLC, CRC and high-grade serous OC	Combo	U.S./Australia/Canada/China/France/Israel/ Japan/Korea/Poland/South Africa/Spain
			1	Solid tumors	Mono/Combo	China
			1	Advanced solid tumors	Mono/Combo	U.S./Australia/Canada/China/France/Israel/ Japan/Korea/Poland/South Africa/Spain
OR502	LILRB2 mAb	OncoResponse, Inc.	1/2	Advanced/metastatic disease not amenable to local therapy with curative intent solid tumor, CSCC or PROC	Mono/Combo	U.S.
JTX-8064	LILRB2 mAb	Jounce Therapeutics	1/2	Advanced Refractory Solid Tumor Malignancies	Mono/Combo	U.S.
SPX-303	LILRB2/PDL1 bsAb	SparX Biotech (Jiangsu) Co., Ltd.	1/2	Solid tumors	Mono	China
			1	Solid tumors	Mono	U.S.
NGM707	LILRB1/LILRB2 bsAb	NGM Biopharmaceuticals	1/2	Solid tumors	Combo	U.S./Chinese Taiwan/Korea
IOMX-0675	LILRB1/LILRB2 bsAb	iOmx Therapeutics	1/2	Advanced solid tumors	Mono	Spain
IO-108	LILRB2 mAb	Immune-Onc Therapeutics	1b	Solid tumors	Mono/Combo	U.S.
			1	Solid tumors	Mono/Combo	China
ES009	**LILRB2 mAb**	**Our Group**	**1**	**Metastatic solid tumors**	**Mono**	**Australia**
CHS-1000	LILRB2 mAb	Coherus Oncology	1	Solid tumors	Mono/Combo	U.S.
CDX-585	LILRB2/PDL1 bsAb	Celldex Therapeutics	1	Solid tumor cancer excluding primary central nervous system tumors	Mono	U.S.
BMS-986406	LILRB2 mAb	Bristol-Myers Squibb	1	Advanced solid tumors	Mono/Combo	US/Argentina/Belgium/Japan/Korea/Spain
IOS-1002	LILRB1/LILRB2/KIR3DL1 msAb	ImmunOs Therapeutics	1	Solid tumors	Mono/Combo	Australia
AK150	LILRB1/LILRB2/CSF1R msAb	Akeso Biopharma	1	Solid tumors	Mono	China

Source: Clinicaltrials.gov, CIC

OC

OC is a malignant tumor that forms on the ovaries. OC was the third most common gynecological cancer globally in 2024, with a global incidence of 338.7 thousand cases. Approximately 70% of OC patients are in advanced stages, with a five-year survival rate of only 17%. In China, OC incidence was 62.4 thousand in 2024 and is expected to reach 67.6 thousand cases in 2035.

Treatment Paradigm

In the U.S. and in China, platinum-based chemotherapy with or without bevacizumab is the core 1L treatment. However, platinum resistance is an important reason leading to treatment failure of OC patients. Approximately 50% to 70% of the OC patients with 1L treatment complete remission relapse within 12 to 18 months. Patients with persistent disease or progression during 1L treatment are treated with 2L approaches depending on whether they are platinum-sensitive, i.e., OC that recurs more than six months after completing 1L platinum-based chemotherapy, or platinum-resistant, i.e., OC that recurs less than six months after completing 1L platinum-based chemotherapy. For platinum-resistant ovarian cancer ("**PROC**") patients, responsiveness to the subsequent platinum-based chemotherapy regimen is less than 30%. Non-platinum monotherapy or combined chemotherapy with anti-angiogenic targeted agents is therefore recommended as resistant disease/recurrence therapy. The need for PROC drugs and other therapies that can achieve better efficacy and improve prognosis of OC patients remains high. For platinum-sensitive ovarian cancer patients, platinum-based monotherapy or combined chemotherapy or bevacizumab is recommended as resistant disease/recurrence therapy, followed by PARP inhibitor or bevacizumab maintenance therapy.

CRC

CRC is the third most prevalent cancer globally, with annual incidence of 2,012.9 thousand cases in 2024, which is expected to reach 2,628.2 thousand cases by 2035. For further details of CRC and its treatment paradigm, see "— China's VEGF/DLL4 BsAb Market — CRC."

GLOBAL AND CHINA'S SIRPα/TAA BSAB MARKET

Overview

SIRPα is a transmembrane protein that binds to CD47 to convey a "don't eat me" signal, inhibiting tumor phagocytosis by macrophages and evading macrophage-mediated immune responses. SIRPα is mainly found on myeloid cells, while CD47 is widely expressed. This makes SIRPα a potentially safer and more effective therapeutic target than CD47, as it may cause less toxicity while still blocking the CD47-SIRPα pathway.

Antibodies targeting SIRPα/CLDN18.2 are guided to CLDN18.2-expressing cancer cells to promote phagocytosis by the local macrophages. CLDN18.2 has limited expression in normal tissues and has a medium to high expression rate among major gastrointestinal cancers, including GC and PDAC. The tumor-selective feature and distribution of CLDN18.2 across some of the most aggressive cancers make it an attractive candidate for the development of immunotherapy especially for gastrointestinal cancers.

Competitive Landscape

As of the Latest Practicable Date, there were 20 SIRPα-targeted drug candidates under clinical development globally and 12 in China, one of which was SIRPα/TAA bsAb. As of the Latest Practicable Date, there was no approved SIRPα/CLDN18.2 bsAb and no SIRPα/CLDN18.2 bsAb under clinical development worldwide. Our Group was one of the only two companies with SIRPα/TAA bsAbs under preclinical studies as of the same date.

GC

GC is the sixth most common cancer globally and the fifth most common cancer in China. It is also the third most deadly cancer worldwide. The prognosis of GC patients is poor as GC is often diagnosed at an advanced stage. The incidence of GC was 864 thousand cases and 348 thousand cases globally and in China in 2024. GC can be classified into HER2-positive and HER2-negative GC, with the latter accounting for over 80% of total GC cases. Around 50% of the patients show medium to high expression of CLDN18.2, making it a promising target for treatment of GC.

Treatment Paradigm

The standard treatments of advanced GC in the U.S. and China primarily comprise chemotherapy, targeted therapy such as HER2-directed drugs and anti-angiogenic drugs, and ICIs. There are limited targeted drugs in the existing treatment paradigm of advanced GC and immunotherapy such as ICIs has only modest efficacy.

In the U.S. and in China, 1L treatment options involve combination therapy regimens, including doublet chemotherapy plus HER2 mAb trastuzumab with or without PD-(L)1 inhibitor for advanced HER2-positive GC and doublet chemotherapy with or without PD-(L)1 inhibitor for advanced HER2-negative GC. Despite the promising results of pembrolizumab in combination with trastuzumab and chemotherapy for HER2-positive advanced GC, approximately 30% of patients do not respond to this treatment. Similarly, while pembrolizumab plus chemotherapy has demonstrated efficacy in HER2-negative advanced GC, nearly 50% of the patients does not respond to this regimen. This highlights the significant unmet need and substantial market opportunity for the development of innovative therapies to improve outcomes for patients with advanced GC, especially for HER2-negative advanced GC. Treatments in the 2L setting include chemotherapy with or without anti-angiogenic mAb ramucirumab and single-agent chemotherapy.

PDAC

The incidence of pancreatic cancer was 534.7 thousand cases and 125.0 thousand cases globally and in China, respectively, in 2024. PDAC is the most prevalent type of pancreatic cancer, accounting for around 80%–90% of total pancreatic cancer cases with a five-year survival rate of less than 8%. Pancreatic cancer remains a formidable challenge due to its often late-stage diagnosis, poor prognosis, and unique characteristics that render many targeted therapies ineffective. The positive expression of CLDN18.2 in patients with primary PDAC was 94.6%, making it a promising target to potentially revolutionize the landscape of PDAC treatment.

Treatment Paradigm

For locally advanced PDAC, in the U.S. and in China, preferred 1L treatment options include (i) FOLFIRINOX, (ii) gemcitabine plus albumin-bound paclitaxel, and (iii) liposomal irinotecan plus 5-FU, leucovorin and oxaliplatin. For PDAC with metastatic disease, which accounts for around 40% of the PDAC patients, in the U.S., preferred 1L treatment options include (i) FOLFIRINOX, (ii) NALIRIFOX, and (iii) gemcitabine plus albumin-bound paclitaxel. In China, recommended 1L treatment options include (i) gemcitabine plus nab-paclitaxel with or without nimotuzumab, (ii) FOLFIRINOX, (iii) S-1 monotherapy and (iv) platinum-based regimen. However, many patients develop resistance to these chemotherapies following 1L therapy, while subsequent treatment options are suboptimal. There are high unmet medical needs for more effective therapies for advanced PDAC. Although recent advancements in immunotherapy have led to notable improvements in survival rates for PDAC patients, it has demonstrated relatively limited clinical benefits and a high likelihood of AEs, indicating the necessity for innovative approach in targeting PDAC.

GLOBAL AND CHINA'S MACROPHAGE-BASED DRUG DISCOVERY PLATFORM

Macrophages are a major component of the TME and orchestrate various aspects of anti-tumor immunity. Macrophage activity is controlled by both positive "eat-me" and negative "don't-eat-me" signals. Upon full activation, macrophages can mediate phagocytosis against tumor cells, and assist in promoting tumor-specific adaptive immune responses by remodeling immunosuppressive TME and increasing T cell-mediated cytolysis. Activated macrophages can release a slew of cytokines and chemokines to recruit T cells into the TME, effectively inflaming "cold" tumors into "hot" tumors. Additionally, macrophages can present tumor-associated antigens to T cells, thereby activating a T cell-mediated response against tumor cells.

The development of macrophage-based drug discovery platforms represents a paradigm shift from conventional BiTE platforms. Despite their proven efficacy in blood cancers, conventional CD3-based BiTEs present significant safety concerns, including severe CRS, and have showed limited clinical efficacy in most of solid tumors to date. Bispecific macrophage engagers, on the other hand, activate macrophages and enhance their ability to phagocytize (i.e., engulf and destroy) tumor cell, while simultaneously binding to TAAs on the surface of tumor cells for greater immune response specificity. Compared to BiTEs, whose rapid T cell activation brings significant risks of severe inflammatory response such as CRS, bispecific macrophage engagers are less likely to cause cytokine storms or other acute and severe AEs as they induce a more targeted and controlled immune response. Furthermore, bispecific macrophage engagers have showed promising potential for the treatment of solid tumors, especially cold tumors with high infiltration of TAMs.

As such, macrophage-based drug discovery platforms are expected to offer new options for cancer patients who do not respond to existing cancer immunotherapies, by modulating TAM and reprogramming the TME. The promising efficacy of bispecific macrophage engager platform is further exemplified by the active licensing arrangements across the globe. For example, in January 2022, Dren Bio, Inc. entered into a research collaboration and license agreement with Pfizer Inc. to advance the discovery and development of antibodies using Dren Bio's proprietary Targeted Myeloid Engager and Phagocytosis Platform. In March 2023, Macomics Ltd., the developer of the ENIGMAC platform also entered into collaboration agreement with Ono Pharmaceutical Co., aiming to develop cancer immunotherapies based on antibody candidates identified through the ENIGMAC platform that focuses on macrophages. In December 2023, the Group entered into a strategic partnership with Astellas to collaborate on the novel bispecific macrophage engager programs derived from the Group's BiME® platform.

REPORT COMMISSIONED BY CHINA INSIGHTS CONSULTANCY

In connection with the [**REDACTED**], we have engaged China Insights Consultancy to conduct a detailed analysis and prepare an industry report on the major markets for which our drug candidates are positioned. China Insights Consultancy is an independent global market research and consulting company that provides market research on a variety of industries including biotechnology. We have agreed to pay China Insights Consultancy a total fee of RMB0.75 million for the preparation of the CIC Report, and we believe that such fees are consistent with the market rate. The payment of such amount was not contingent upon our successful [**REDACTED**] or on the results of the CIC Report. Except for the CIC Report, we did not commission any other industry report in connection with the [**REDACTED**].

The market projections in the CIC Report were based on the following key assumptions: (i) the overall social, economic and political environment in China is expected to remain stable during the forecast period; (ii) China's economic and industrial development is likely to maintain a steady growth trend over the next decade; (iii) related key industry drivers are likely to continue driving the growth of the market during the forecast period; and (iv) there is no extreme *force majeure* or industry regulation in which the market may be affected dramatically or fundamentally. The reliability of the CIC Report may be affected by the accuracy of the foregoing key assumptions.