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 Frost & Sullivan (the "Frost & Sullivan Report"). We engaged Frost & Sullivan to prepare the Frost & Sullivan Report, an independent industry report, in connection with the* [REDACTED]. *The information from official government sources has not been independently verified by us, the Joint Sponsors, the* [REDACTED], *the* [REDACTED], *the Joint* [REDACTED], *the* [REDACTED], *the* [REDACTED], *any of the* [REDACTED], *any of their respective directors and advisers, or any other persons or parties involved in the* [REDACTED], *and no representation is given as to its accuracy.

GLOBAL AND CHINA'S PHARMACEUTICAL MARKETS

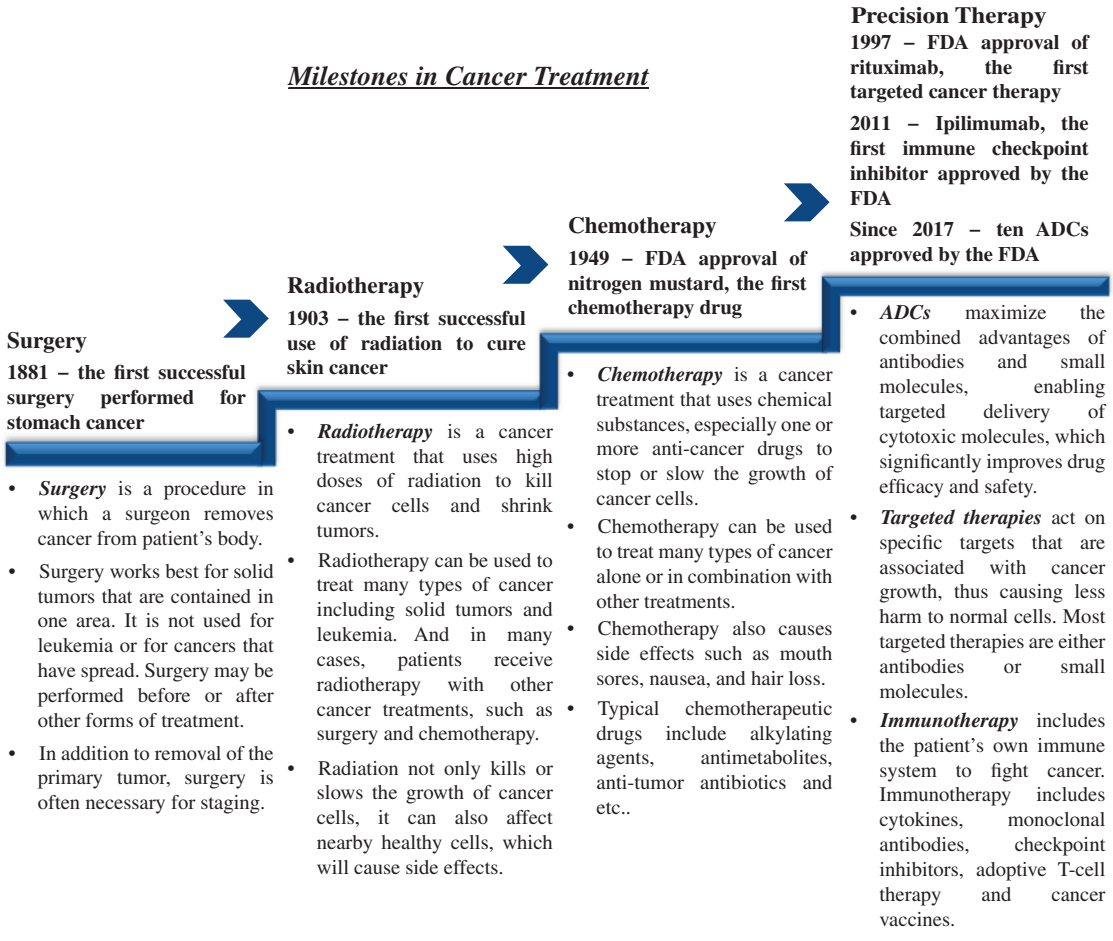
The global and China's pharmaceutical markets have witnessed significant growth in recent years and are projected to grow at a rapid pace over the next decade. Driven by an aging population, growing R&D expenditure and technology advancements, the global pharmaceutical market grew from US$1,208.4 billion in 2017 to US$1,495.0 billion in 2022 at a CAGR of 4.3% and is projected to reach US$2,090.8 billion in 2030 at a CAGR of 4.3% from 2022. Meanwhile, the pharmaceutical market in China grew from from RMB1,430.4 billion in 2017 to RMB1,554.1 billion in 2022 at a CAGR of 1.7% and is anticipated to reach RMB2,624.5 billion in 2030 at a CAGR of 6.8% from 2022. Once dominated by generic drugs, China's pharmaceutical landscape has undergone significant development with the innovative drug market expanding rapidly in recent years. Following the implementation of favorable government policies for drug innovation, China has witnessed a significant growth in NDAs granted by the NMPA for innovative drugs, from one in 2017 to 47 in 2021. Accordingly, China's patented drug market grew from RMB799.0 billion in 2017 to RMB958.9 billion in 2022 at a CAGR of 3.7%, and is projected to grow at a faster pace and reach RMB1,972.5 billion by 2030 at a CAGR of 9.4% from 2022.

THE ONCOLOGY DRUG MARKET

Overview

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. Cancer is the leading cause of mortality worldwide with 10.5 million deaths globally and 2.9 million deaths in China in 2022, and its disease burden is expected to climb as a result of population growth and aging. Global cancer incidence was 20.2 million in 2022 and is projected to reach 24.5 million in 2030. In China, the total cancer incidence was 4.8 million in 2022 and is expected to reach 5.8 million in 2030.

Cancer treatment has evolved rapidly over the past few decades. As illustrated in the diagram below, the landscape of cancer treatment has progressed from surgery and indiscriminate cytotoxic treatments, such as radiotherapy and chemotherapy, to precision therapy, with antibody-based drugs including mAbs, bsAbs and ADCs being a major category. Notably, ADCs are one of the fastest-growing treatment modalities in recent years, progressing from a late-line treatment in selected blood cancers to a promising early-line therapeutic modality for broader solid tumor indications and beyond.



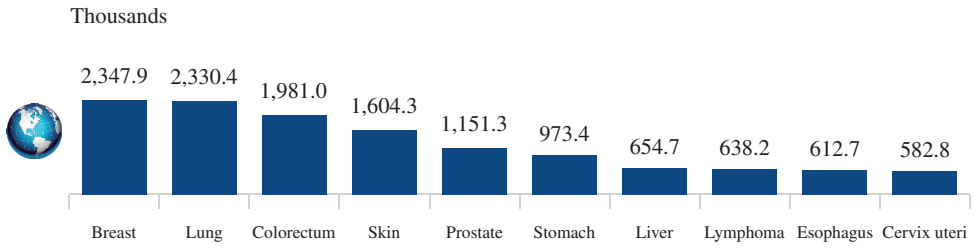
Source: Literature research, Frost & Sullivan

In 2022, targeted therapy and immunotherapy were the two largest oncology drug classes globally with a 61.3% and 24.5% market share, respectively, followed by chemotherapy (14.2%). In China, the development of targeted therapy and immunotherapy has lagged behind other major markets such as the U.S. In 2022, China's oncology drug market was dominated by chemotherapy with a 54.3% market share, while targeted therapy and immunotherapy only occupied 37.0% and 8.7% of the market, respectively.

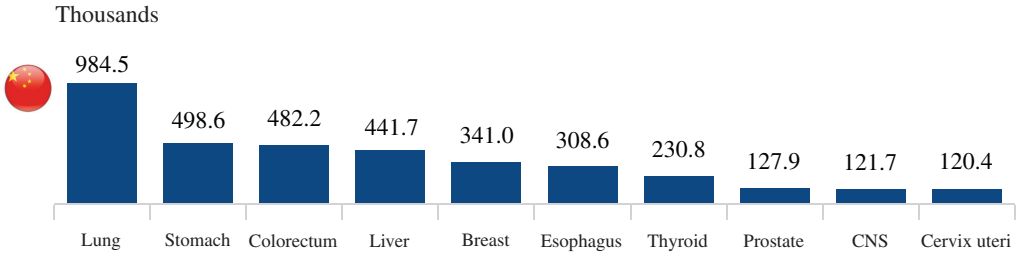
Top Ten Cancer Types Globally and in China

As illustrated in the charts below, China has an overlapping but different profile of top ten cancers by incidence compared to that globally, with LC, GC and CRC 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 LC, indicating vast addressable patient populations for these cancer types both globally and in China.

Top 10 Cancers by Incidence Globally, 2022



Top 10 Cancers by Incidence China, 2022



Source: Globocan, IARC, NCCR, Frost & Sullivan

Market Size

The global and China's oncology drug markets have expanded rapidly in recent years. The global oncology drug market rose from US$110.6 billion in 2017 to US$205.1 billion in 2022 at a CAGR of 13.1% and is projected to reach US$458.6 billion in 2030 at a CAGR of 10.6% from 2022. The oncology drug market in China grew from RMB139.4 billion in 2017 to RMB233.6 billion in 2022 at a CAGR of 10.9% and is forecasted to continue its strong growth, reaching RMB586.6 billion in 2030 at a CAGR of 12.2% from 2022.

Market Drivers and Future Trends

The growth of the oncology drug market is driven primarily by the following factors:

Expanding Patient Pool with Significant Medical Needs. Together with population growth and aging demographic, advances in early-stage diagnosis and improving survival rates have substantially increased the oncology patient pool, which has in turn driven the expansion of the oncology drug market globally. In China, the outcomes of oncology patients, despite the improvements witnessed in recent years, still lag behind those in developed countries. In part due to the relatively limited availability of more advanced treatment modalities such as ADCs, the five-year survival rate of cancer patients in China (40.5%) was substantially lower compared to those in the U.S. (67.1%) in 2015. Survival for advanced cancer patients, in particular, remains poor despite recent advances in targeted and immunotherapies, as existing modalities are limited by drug resistance and risks of serious side effects, with limited effective treatment options available to late-line patients. This indicates a significant medical need for more innovative therapies to improve cancer prognosis and outcome. As set out in its Healthy China Action (2019-2030) (《健康中國行動(2019-2030)》), China is committed to raising the overall five-year survival rate of cancer patients to 46.6% by 2030.

Increasing Medical Expenditure. The global economy experienced rapid growth in the past two decades. Higher disposable income per capita has made it easier for patients to afford treatments. In particular, medical expenditures per capita in China increased from approximately RMB3,756.7 in 2017 to RMB5,348.1 in 2021, having expanded at a robust CAGR of 9.2%. This factor is expected to continue enhancing Chinese patients' ability and willingness to pay for more advanced and expensive treatments options, especially for life-threatening diseases like cancers.

Improved Reimbursement Environment. Enhancing the affordability of medical treatments has increasingly become a policy priority for regulators worldwide. Recent reforms in government-sponsored medical insurance schemes in China, in particular, have lowered the cost and improved the affordability of oncology treatments to Chinese residents. Following the implementation of the dynamic adjustment mechanism in 2017, the national reimbursement drug list (NRDL) had witnessed a rapid growth in the number of oncology drugs admitted via price negotiation, from only two in 2016 to 14 in 2022 while showing increased flexibility and shortened time intervals between each round of negotiation. This has substantially improved patients' access to potentially life-saving oncology medicines, which drives demand and, in turn, growth of the oncology drug market.

Favorable Government Policies Driving Innovation. Government support has driven and will continue to drive oncology research and development. One of China's major goals is to reshape the industry from developing "me too" or "me better" drugs and relying on drug in-licensing to one that fosters and promotes end-to-end innovation. The "Fourteenth Five-Year Plan for National Economic and Social Development of the PRC and the Outline of Vision Goals for 2035 (《中華人民共和國國民經濟和社會發展第十四個五年規劃和2035年遠景目標綱要》)" released in 2021 continues to emphasize the central role of innovation in China's

modernization progress, and the significance of R&D breakthrough in medical science. After launching its priority review mechanism in 2016, the NMPA has further streamlined NDA review procedures, which contributed to a significant growth in NDAs granted for Class 1 innovative drugs. For more details on China's recent healthcare reform, see "Regulatory Overview – Laws and Regulations in Relation to New Drugs."

The oncology drug market is expected to be influenced by the following trends:

Shifting Treatment Paradigm and Emergence of New Modalities. As a global trend, an increasing number of targeted therapy and immunotherapy drugs with improved clinical efficacy and safety have displaced or been added alongside chemotherapy as standard treatments. Deepening insights into cancer biology and advances in engineering technologies have propelled the development of novel treatment modalities such as ADCs that improve upon the clinical efficacy and safety of more traditional therapies. Despite their improved clinical benefits, the approved novel treatment modalities, such as TROP2 and HER2 ADCs, are still limited by drug resistance and notable safety concerns, leaving many patients underserved. Therefore, there is a significant unmet need for emerging modalities with differentiated or better efficacy and safety profiles, which are expected to transform the treatment paradigm of many cancer indications. In China, the market shares of targeted therapies and immunotherapies are forecasted to reach 45.9% and 39.9% by 2030, respectively, overtaking chemotherapy as the major cancer treatment modalities.

Increasing Use of Combination Therapy. Combination therapy, which uses two or more therapies with distinct mechanisms of actions, has become increasingly common as it can target cancers from multiple approaches simultaneously with potentially superior efficacy relative to monotherapies. The development of novel treatment modalities is expected to result in a greater number and variety of combination treatments.

Precision Medicine. Due to tumor heterogeneity, precision medicine tailored to each patient is critical for effective cancer treatment. Advances in genomic profiling have enabled more accurate characterization of a patient's tumor. This, combined with a deeper understanding of disease biology, has empowered the development of precision therapies, highlighted by an increasing number of targeted therapy and immunotherapy based on targetable biomarkers. Some of these biomarker-driven therapies have demonstrated robust clinical benefits across multiple tumor types that share the same genomic alterations, leading to broad indication approvals, such as PD-(L)1 inhibitors that target patients with certain immunotherapy biomarkers and ADCs that target TROP2 and HER2 overexpression across a wide range of solid tumors. Rapidly evolving genomic technologies are expected to accelerate the translation of biomarker discoveries into novel targeted therapy and immunotherapy that may continue to transform treatment paradigm.

Managing Cancer as a Chronic Disease. With therapeutic advances over the years, many cancers can now be controlled with treatments for months or even years. Patients previously without effective treatments, especially those diagnosed at an advanced stage, are now more likely to benefit from increasing treatment options. The need for managing cancer as a chronic disease effectively calls for innovative therapies with optimized balance between safety and efficacy, as well as differentiated mechanisms of action that may overcome drug resistance to existing treatments to prolong disease control.

THE ANTIBODY-BASED DRUG MARKET

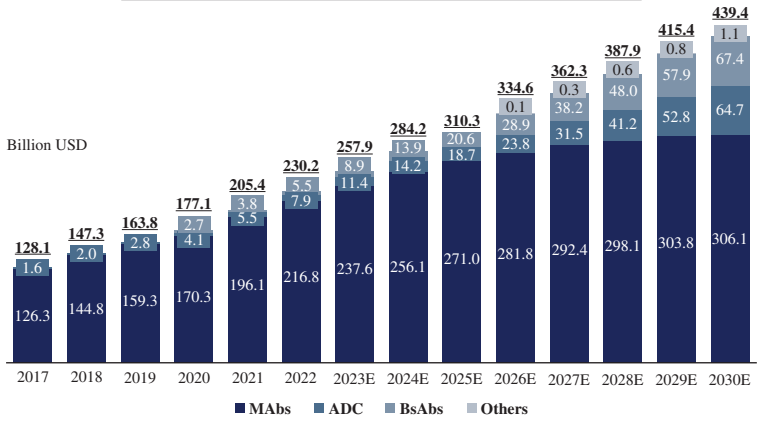
The antibody-based drug market covers antibody-based drugs for oncology and non-oncology indications. Antibody-based drugs are the largest category of biologics with generally higher efficacy and fewer side effects than conventional chemical drugs, such as chemotherapy, as antibody-based drugs are designed to engage specific molecular targets involved in disease pathogenesis, with potentially reduced harmful effects on non-target cells. Key categories of antibody-based drugs include mAbs, ADCs and bsAbs.

Global and China's Market Size of Antibody-based Drugs

The global antibody-based drug market grew at a CAGR of 12.4% from US$128.1 billion in 2017 to US$230.2 billion in 2022. It is expected to continue its rapid growth in the coming years, reaching US$439.4 billion in 2030 at a CAGR of 8.4%. Driven by a growing patient population, strong government support and continuous R&D activities, the antibody-based drug market in China grew from RMB11.8 billion in 2017 to RMB75.9 billion in 2022 at a CAGR of 45.1% and is expected to reach RMB479.3 billion in 2030 at a CAGR of 25.9% from 2022. The charts below show the growth of the global and China antibody-based drug markets.

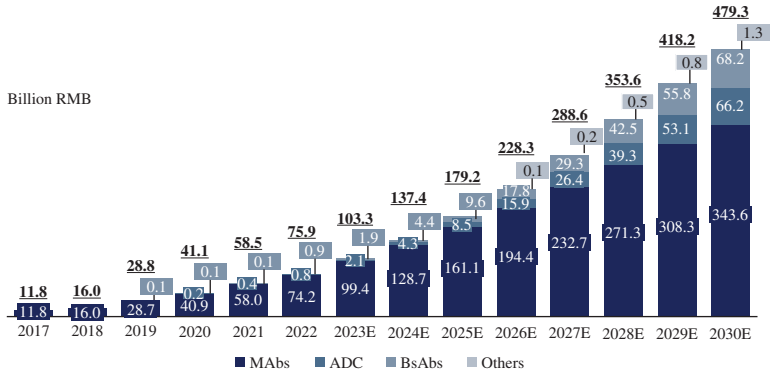
Historical and Forecasted Market Size of Antibody-based Drug Market Globally, 2017-2030E

CAGR	ADC	MAbs	BsAbs	Others	Total
2017-2022	37.3%	11.4%	98.3%	NA	12.4%
2022-2030E	30.0%	4.4%	36.9%	NA	8.4%



Historical and Forecasted Market Size of Antibody-based Drug Market in China, 2017-2030E

CAGR	ADC	MAbs	BsAbs	Others	Total
2017-2022	NA	44.5%	N/A	N/A	45.1%
2022-2030E	72.8%	21.1%	72.8%	N/A	25.9%



Source: FDA, NMPA, annual report, MOHRSS, Frost & Sullivan

As of the Latest Practicable Date, mAbs were the largest class of antibody-based drugs in China, with a market size of RMB74.2 billion in 2022. New generations of antibody-based drugs such as ADCs and bsAbs hold vast therapeutic potential. The ADC and bsAb markets are expected to experience substantial growth in the near future, faster than the overall antibody-based drug market, as more drug candidates obtain approval.

Comparison of Different Antibody-based Drugs

Among the major types of antibody-based drugs, ADC is an advanced modality that is differentiated from traditional chemotherapy and targeted drugs, as well as other antibody-based therapies. By combining the target selectivity of antibodies with the cell-killing potency of highly cytotoxic drugs, ADCs enable the selective delivery of cytotoxic drugs to the tumor. Compared to chemotherapy, ADCs potentially have a wider therapeutic window as they enable targeted delivery of payloads with much higher cytotoxicity to the tumor site than standard chemotherapy drugs, while reducing toxicity to healthy cells. Compared to other antibody-based drugs and targeted therapies, which heavily rely on the expression and biological effects of the target antigen(s), ADCs can potentially bring enhanced efficacy and overcome treatment resistance as they primarily exert anti-tumor effect via the cytotoxic payloads they are equipped with. This differentiated mechanism allows ADCs to better overcome low or heterogeneous antigen expression in tumors, which is a major cause of treatment resistance to other antibody-based drugs and targeted therapies. The potential of ADCs to overcome treatment resistance is supported by the approved use of ADCs for late-line patients who have failed other antibody-based drugs or targeted therapies.

A comparison of ADCs, bsAbs and mAbs is set forth in the table below:

	ADC	BsAb	MAb
Characteristic	Composed of an antibody linked to a biologically active cytotoxic drug.	Simultaneously bind to two different epitopes or antigens.	Made by identical immune cells that are all clones of a unique parent cell.
Advantages	Compared to chemotherapy, ADCs potentially have a wider therapeutic window as they enable targeted delivery of payloads with much higher cytotoxicity than standard chemotherapy drugs to the tumor site while reducing toxicity to healthy cells; Compared to other antibody-based drugs and targeted therapies, ADCs potentially have (i) enhanced efficacy as ADCs exert anti-tumor effects primarily via highly potent payloads and bystander effect, which may overcome low or heterogeneous antigen expression in tumors; (ii) more options to target as ADCs do not necessarily require the target antigen to have any biological effects, unlike mAbs.	BsAbs's dual specificity potentially allows for (i) enhanced tumor killing via redirecting immune cells to tumor cells, (ii) concurrent blockade of distinct pathways with unique/overlapping functions, and (iii) increased binding capability by interacting with two different cell-surface targets instead of one.	Proven clinical activity for various diseases, notably cancers and autoimmune diseases.
Limitations	Complex drug design and difficulties in manufacturing to produce ADCs with optimized parameters, including target selection, antibodies, payloads and the payload-linker linkage.	Complexity in manufacturing and selecting the optimal molecular design to fit the proposed mechanisms of action; Potentially lower dosing flexibility due to the fixed ratio, i.e., relative dose, of the two component antibodies.	More likely to encounter drug resistance due to the heterogeneous antigen distribution within the same tumor, or experience low treatment response rates due to heterogeneous antigen expression between tumors from different patients.

Source: Literature review, Frost & Sullivan

The ADC Market

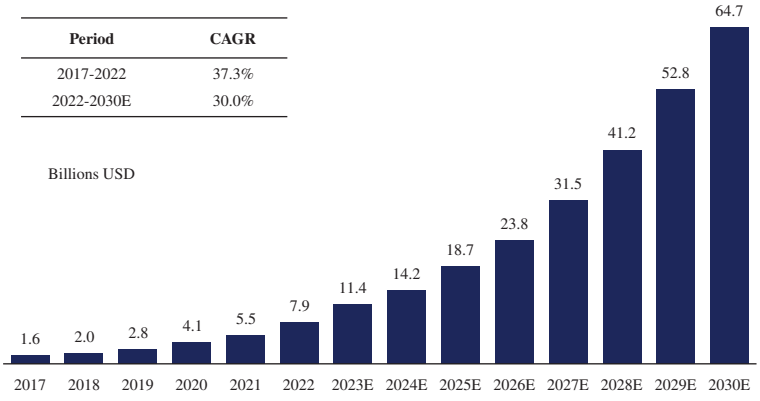
Overview

ADCs are one of the fastest-growing treatment modalities for cancer. They combine the target selectivity of antibodies and the cell-killing potency of highly cytotoxic drugs. Classic chemotherapy, the mainstay of anti-cancer treatment, demonstrates limited selectivity against cancer cells, frequently resulting in intolerable systemic toxicity. Like guided missiles, ADCs are designed to utilize an antibody to deliver cytotoxic drugs selectively to tumor cells. This combinatorial design potentially reduces off-target toxicity while allowing the use of highly potent cytotoxic drugs that would otherwise be intolerable in systemic therapies, thereby leading to improved therapeutic window and efficacy.

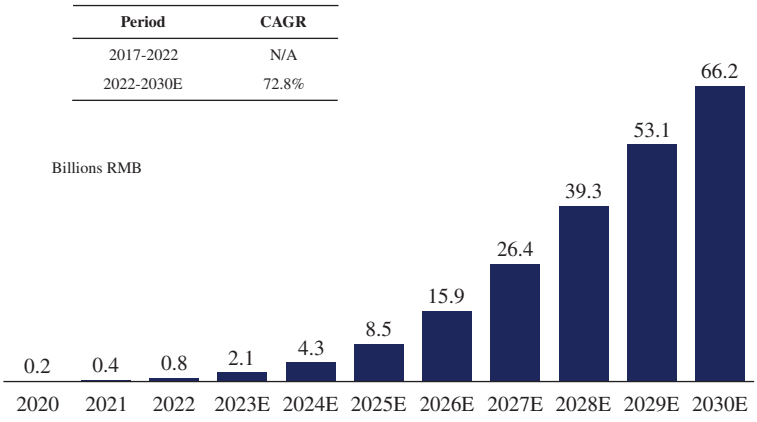
Global and China's Market Size of ADCs

The global ADC market size grew rapidly from US$1.6 billion in 2017 to US$7.9 billion in 2022 at a CAGR of 37.3% and is projected to continue its robust growth at a CAGR of 30.0% from 2022 to 2030. China's ADC market started to grow, following the approval of the first ADC, Kadcyla, by the NMPA in 2020, and is expected to increase from RMB0.8 billion in 2022 to RMB66.2 billion at a CAGR of 72.8%.

Historical and Forecasted Global ADC Market Size, 2017-2030E



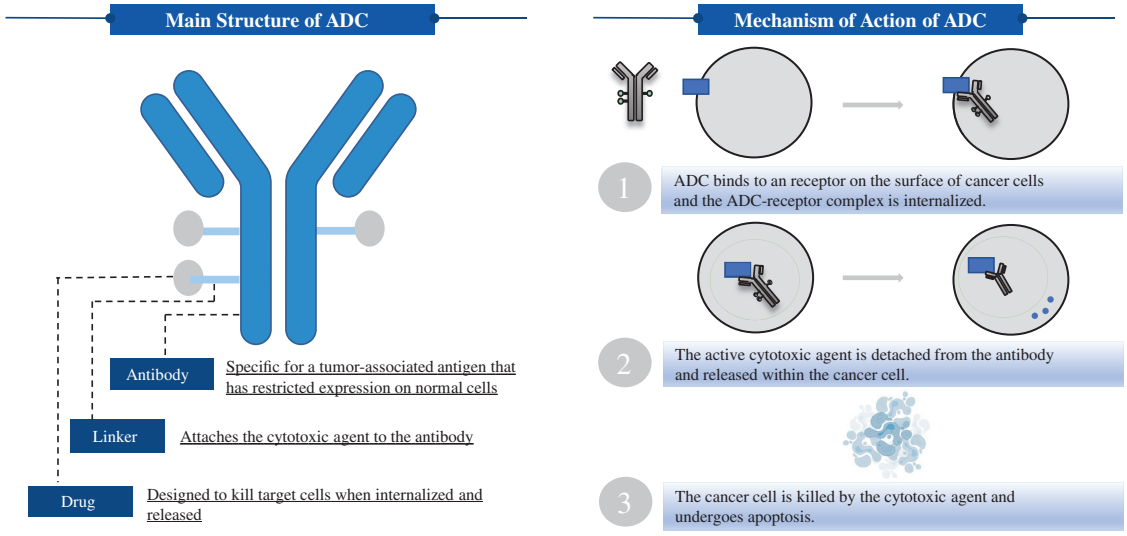
Historical and Forecasted China ADC Market Size, 2020-2030E



Source: FDA, NMPA, annual report, MOHRSS, Frost & Sullivan

ADC Drug Design

ADCs comprise three core components: an antibody that binds to a specific target, a cytotoxic agent known as the payload, and a linker connecting the two. These components can be designed to influence the pharmacological and clinical profiles of the ADC. The following diagram illustrates an ADC's structure and its canonical mechanism of action:



Source: Frost & Sullivan

Despite their vast therapeutic potential, early generations of ADCs faced various challenges, including toxicities and suboptimal efficacy that stymied numerous ADC development programs from the 1980s to the 2000s. These challenges were largely associated with the complex drug design of ADCs, which requires thoughtful combination of antibodies, linkers and payloads in the context of a defined target, cancer indication and its associated microenvironment.

Major considerations in ADC design are discussed below:

- Antibody and Target Selection. The target affinity, internalization efficiency, solubility, circulation half-life, and immunogenicity of the antibody are important factors to consider. An ideal antibody target should be a tumor-associated antigen, a cell surface protein preferentially expressed in tumors versus healthy tissues. Examples of clinically validated targets include TROP2, HER2 and Nectin-4, which are overexpressed in a broad range of cancers.

- Payloads. The cytotoxic potency, mechanism of action and cell permeability of the payload are key features for consideration. Most FDA-approved ADCs carry payloads with much higher cytotoxicity than standard chemotherapy drugs. These payloads usually trigger cell death by interrupting DNA replication, e.g., topoisomerase I (TOPO1) inhibitors, or by disrupting the cell's skeleton, e.g.,

microtubule destabilizers. The cell permeability of payloads determines how well the detached payloads can diffuse from within cells that express the target antigen into neighboring cells, where the payload can exert a cytotoxic effect independent of target antigen expression, i.e., bystander killing.

- Linker. Linkers dictate how and when the payload is released from the ADC and can be broadly categorized as non-cleavable and cleavable. Non-cleavable linkers are associated with less off-target toxicity and bystander effect as payload release occurs only after ADC internalization and intracellular antibody degradation, whereas cleavable linkers tend to offer greater versatility as diverse biological cues commonly found in tumor microenvironment, such as low pH, can be used to trigger payload release. Both types of linkers have their respective advantages and limitations and each can be modified to balance efficacy and undesired toxicity. For example, Kadcyla's MCC linker, due to its non-cleavable nature, prevents the linker-payload moiety from crossing the cell membrane, which limits bystander effect and potentially contributes to drug resistance. Alternative linkers, such as the cleavable Val-Cit linker used by A166, potentially overcome such drug resistance mechanism by enabling the linker to be degraded, which allows payload release and diffusion across cell membrane to exert bystander effect.

- DAR and Conjugation Technology. Another important factor to consider when designing ADCs is DAR, i.e., the number of payloads conjugated to one antibody. Attaching too few payload molecules may result in insufficient efficacy, while attaching too many will destabilize the ADC, altering its PK profile, inducing plasma clearance and increasing systemic toxicity. Conjugation technology is another major factor in the successful design of ADCs. Compared to site-specific conjugation technology, non-site-specific conjugation technology offers greater ease of use but results in a heterogeneous mixture of ADCs with variable numbers of payloads attaching to each antibody. This product heterogeneity can lead to inconsistent PK profiles that may adversely affect the efficacy and safety of the drug. In contrast, by engineering specific sites onto mAbs for connecting payload-linker groups, site-specific conjugation technology enables the generation of homogeneous ADCs with a pre-specified, desired DAR, which potentially improves ADC activity.

The complex design of ADCs also poses a high demand on manufacturing capabilities, as it requires advanced manufacturing suites with specialized equipment, deep analytical know-how and careful handling techniques to accurately characterize each of the ADC components and ensure the purity, stability and DAR of the final product.

The following table illustrates the respective ADC design of SKB264 and A166 alongside that of Trodelvy and DS-1062, two TROP2 ADCs at phase 3 stage or beyond, as well as Kadcyla, Aidixi and Enhertu, three FDA and/or NMPA-approved HER2 ADCs as of the Latest Practicable Date.

ADC design of TROP2 ADCs (SKB264, Trodelvy and DS-1062)

	SKB264	**Trodelvy**	**DS-1062**
Antibody	Sacituzumab	Sacituzumab	Datopotamab
Linker	2-methylsulfonyl pyrimidine-containing CL2A linker	Maleimide-containing CL2A linker	GGFG linker
Payload	KL610023, a belotecan derivative	SN-38, a water-soluble metabolite of irinotecan	Deruxtecan, an Exatecan derivative
Conjugation	Irreversible site-specific methylsulfonyl pyrimidine-thiol conjugation	Reversible site-specific maleimide-thiol conjugation	Reversible site-selective maleimide-thiol conjugation
Overall DAR	7.4	7.6	4
Major differentiation of SKB264 vs. Trodelvy/DS-1062	/	• SKB264's improved plasma stability due to irreversible linker-mAb conjugation and differentiated payload structure	• SKB264's favorable ADC hydrophilicity even at a higher DAR value due to the more hydrophilic CL2A linker • SKB264's minimal risk of ILD toxicity associated with KL610023

ADC design of HER2 ADCs (A166, Kadcyla, Aidixi and Enhertu)

	A166	Kadcyla	Aidixi	Enhertu
Antibody	Trastuzumab	Trastuzumab	Disitamab	Trastuzumab
Linker	Val-Cit linker	MCC linker	Val-Cit linker	GGFG linker
Payload	Duo-5, a MMAF derivative and a highly toxic tubulin inhibitor	DM1, a maytansine derivative and a highly toxic tubulin inhibitor	MMAE, a highly toxic tubulin inhibitor	Deruxtecan, an Exatecan derivative and a moderately toxic TOPO I inhibitor
Conjugation	Stable site-specific lysine conjugation	Stochastic lysine conjugation	Reversible non-site-specific cysteine conjugation	Reversible site-specific cysteine conjugation
DAR	2	3.5	4	8
Major differentiation of A166 vs. Kadcyla/ Aidixi/Enhertu	/	• A166's greater ADC homogeneity due to site-specific conjugation • A166's bystander effect due to enzyme-cleavable linker with cell membrane permeable payload	• A166's greater ADC homogeneity due to site-specific conjugation • A166's improved plasma stability due to stable linker-mAb conjugation	• A166's minimal risk of ILD toxicity associated with Duo-5 • A166's improved plasma stability due to stable linker-mAb conjugation

Source: Frost & Sullivan

Market Drivers and Future Trends of ADC Development

Advances in ADC Design and Conjugation Technologies. ADCs have recently begun to gain momentum after two decades of trial and error after its first approval in 2000 by the FDA, encouraged by the successful launch of new drugs with outstanding clinical outcomes, such as Enhertu (HER2-directed) and Padcev (Nectin-4-directed) in 2019 and Trodelvy (TROP2-directed) in 2020. In particular, ongoing research on ADC technology and cancer biology is expected to drive the discovery of novel molecular targets and payload molecules,

as well as better linker design and conjugation technologies, potentially yielding new designs that improve the therapeutic effects of ADCs and reduce the toxicity issues that limit the use of currently marketed ADCs. Leveraging the continuous advancement in ADC design and conjugation technologies, with a total of 12 FDA-approved ADCs to date, ADCs have progressed from a late-line treatment in selected blood cancers to a promising early-line therapeutic modality for broader solid tumor indications and beyond.

Expansion of Indications and Treatment Lines. Advancement in ADC technologies is expected to result in a broader range of potential molecular targets and indications, including in non-oncology areas such as autoimmune diseases. ADCs are also expected to enter earlier treatment lines and expand into the early stages of cancers with larger addressable patient populations.

Combination with Other Treatment Modalities. The mechanisms of action of ADCs may synergize with other treatment modalities to potentiate tumor cell killing. For instance, combination therapies with ADCs and immune checkpoint inhibitors have shown promise in clinical studies in enhancing anti-tumor efficacy.

Growing Needs for Fully Integrated Capabilities. The R&D of ADCs requires extensive biological, chemical and manufacturing know-how and capabilities that span across biologics, small molecules and bioprocessing. The increasing development and manufacturing needs for ADCs are expected to benefit biopharmaceutical companies with fully integrated end-to-end capabilities that enable the rapid advancement of ADC candidates.

The BsAb Market

BsAbs are an emerging treatment modality that concurrently binds two distinct epitopes or antigens. Their dual specificity potentially enables multiple synergistic functions previously unattainable by using mAbs alone, while offering reduced treatment cost, simplified treatment regimen/administration and improved safety compared to combination therapies with two mAbs.

Given the promising therapeutic potential of bsAbs, the global market of bsAbs grew at a CAGR of 98.3% from 2017 to 2022 with ten marketed products as of the Latest Practicable Date, and it is expected to further expand to US$67.4 billion by 2030 at a CAGR of 36.9% from 2022. As bsAbs development requires extensive end-to-end capabilities that span from antibody engineering and technology platform to bioprocessing, there were no bsAbs on the market in China until 2020. The bsAb market in China was estimated to be about RMB0.9 billion in 2022 with only three approved products as of the Latest Practicable Date. However, with the maturation of bsAb technology platforms, anticipated launch of more bsAbs and potential indication expansion, the bsAb market in China is expected to increase to RMB68.2 billion in 2030 at a CAGR of 72.8% from 2022.

The MAb Market

MAbs are a major class of targeted therapy that specifically binds to a designated epitope on a target protein. Since their first approval by the FDA in 1986, mAbs have transformed treatment paradigm, enabling many diseases such as cancer to be treated in a more targeted way.

As the predominant treatment modality for various diseases, the global market for mAbs grew rapidly at a CAGR of 11.4% from 2017 to 2022 and is projected to reach US$306.1 billion by 2030 at a CAGR of 4.4% from 2022. The mAb market in China increased at a CAGR of 44.5% from 2017 to 2022 and is forecasted to reach RMB343.6 billion by 2030 at a CAGR of 21.1% from 2022.

GLOBAL AND CHINA'S TROP2 ADC MARKETS

Overview

TROP2 is a transmembrane protein that has essential functions in embryonic and organ development with low expression in normal tissues. Across a broad spectrum of cancers, TROP2 is frequently overexpressed and promotes cancer proliferation, invasion and metastasis.

TROP2 is a clinically valuable ADC target as it is overexpressed with low heterogeneity in a wide range of highly prevalent or hard-to-treat cancers, including advanced tumors with limited actionable targets. TROP2 ADCs have also demonstrated synergistic anti-tumor activity in various preclinical and clinical studies as the backbone of potential combination therapies with other treatment modalities such as chemotherapy, targeted therapy and immunotherapy.

As of the Latest Practicable date, Gilead Sciences' TROP2 ADC Trodelvy was the only approved TROP2-directed drug globally. Despite its promising clinical activity, Trodelvy is associated with severe neutropenia (i.e., a lower-than-normal number of neutrophils in the blood) and severe diarrhea, two serious adverse reactions for which Trodelvy has black box warnings issued by the FDA. Consequently, there is a high unmet need for novel TROP2 ADCs that have limited toxicities while maintaining robust anti-tumor activity.

Addressable Market Size of TROP2 ADCs

The table below highlights the major cancers in which TROP2 is frequently overexpressed. They include some of the most prevalent or hard-to-treat cancers such as BC (including TNBC and HR+/HER2-BC), NSCLC, GC, OC, CRC, urothelial cancer (UC), PC, cervical cancer (CC), castrate-resistant prostate cancer (CRPC), head and neck squamous cell carcinoma (HNSCC), and endometrial cancer (EC), indicating significant market potential for novel TROP2 ADCs. Notably, TROP2 has one of the highest overexpression rates in BC (including TNBC and HR+/HER2- BC) and NSCLC, the lead indications of SKB264. Other

than SKB264, Gilead Sciences' Trodelvy and Daiichi Sankyo's DS-1062 were the only two TROP2 ADCs in phase 3 stage or beyond globally that target the same lead indications as SKB264 as of the Latest Practicable Date. See "– Global and China's TROP2 ADC Markets – Competitive Landscape of the Global TROP2 ADCs Market" for further details.

Indication	Overexpression[1]
BC[2]	80%
NSCLC	64% to 75%
GC	56%
OC	59%
CRC	68%
UC	83%
PC	55%
CC	88.7%
CRPC	89%
HNSCC	42.9%
EC	84%

Notes:

(1) "Overexpression" refers to the proportion of patients with TROP2 overexpression for a given indication;

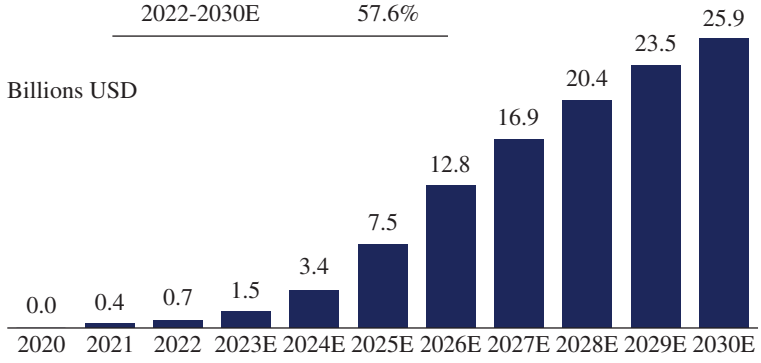
(2) TNBC: 88%; HR+/HER2- BC: significantly higher TROP2 expression than other HER2+ subtypes.

Source: Literature review, Frost & Sullivan

As shown in the charts below, the global TROP2 ADC market was US$0.7 billion in 2022 and is expected to reach US$25.9 billion in 2030 at a CAGR of 57.6% from 2022. The TROP2 ADC market in China is expected to grow, following the approval of the first TROP2 ADC, Trodelvy, by the NMPA in 2022, and is expected to reach RMB23.6 billion in 2030 at a CAGR of 103.0% from 2023.

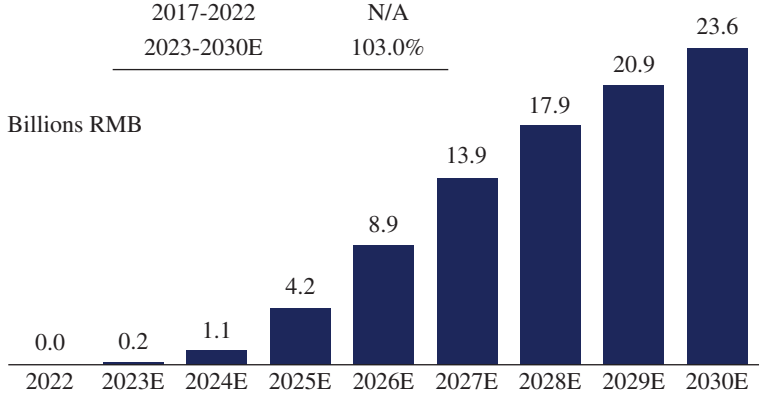
Global TROP2 ADCs Market Size, 2020-2030E

Period	CAGR
2017-2022	N/A
2022-2030E	57.6%



China TROP2 ADCs Market Size, 2022-2030E

Period	CAGR
2017-2022	N/A
2023-2030E	103.0%



Source: FDA, NMPA, annual report, MOHRSS, Frost & Sullivan

TNBC

BC is the most prevalent type of cancer worldwide. TNBC is an aggressive subtype of BC, representing approximately 15% of total BC cases globally and in China. It is characterized by the absence of estrogen, progesterone and HER2 receptors, three actionable targets commonly found in other subtypes of BC. TNBC is associated with a worse prognosis compared to other BC subtypes and about 85% of TNBC patients present with advanced disease at the time of diagnosis, with a five-year survival rate of about 12%. TROP2 is overexpressed in approximately 88% of TNBC patients.

Incidence

Globally, the incidence of TNBC grew from 306.7 thousand in 2017 to 352.2 thousand in 2022 and is projected to reach 408.8 thousand in 2030. In China, the incidence of TNBC increased from 47.3 thousand in 2017 to 51.2 thousand in 2022 and is expected to reach 55.6 thousand in 2030.

Treatment Paradigm

Chemotherapy, immunotherapy and targeted therapy are the recommended treatment options for treating advanced TNBC in the U.S. and China. As of the Latest Practicable Date, Trodelvy was the only approved TROP2 ADC for advanced TNBC in the U.S. and China.

In the U.S., the first-line and beyond (1L+) treatments for advanced TNBC include single-agent chemotherapy or doublet chemotherapy that combines two chemotherapy drugs, chemoimmunotherapy that combines chemotherapy with PD-1 inhibitor for PD-L1-positive (PD-L1+) patients, and poly (ADP-ribose) polymerase (PARP) inhibitor for patients with deleterious BRCA mutations. For adult patients with metastatic TNBC who have received at least two prior therapies with at least one line for metastatic disease, Trodelvy is approved as a 3L+ treatment.

In China, the 1L treatments for advanced TNBC involve either single-agent or doublet chemotherapy. The 2L treatment options consist of single-agent chemotherapy and combination therapy including chemoimmunotherapy with PD-(L)1 inhibitor, doublet chemotherapy and chemotherapy with anti-angiogenic mAb bevacizumab. For patients who progress during or after 2L treatments, 3L+ treatment options include TROP2 ADC Trodelvy, liposome-encapsulated chemotherapy, and PARP inhibitor for patients with deleterious BRCA mutations.

Despite the survival benefits brought by chemoimmunotherapy and PARP inhibitor therapy, they are only beneficial for advanced TNBC patients with PD-L1 expression and deleterious BRCA mutations, representing only 20% and 10-20% of the total advanced TNBC patient population, respectively. Although the recent approval of Trodelvy (TROP2 ADC) as a 3L+ treatment improves survival in heavily pre-treated patients with advanced TNBC, many patients are unresponsive or develop resistance to Trodelvy. Moreover, the FDA issued a black box warning for Trodelvy for severe neutropenia (i.e., a lower-than-normal number of neutrophils in the blood) and severe diarrhea. Consequently, there is a substantial unmet need for safe and effective treatments.

HR+/HER2- BC

HR+/HER2- BC is the most prevalent subtype of BC, accounting for approximately 55% of total BC cases worldwide. About 5-10% of HR+/HER2- BC patients are diagnosed with advanced disease, with a five-year survival rate of about 30%. HR+/HER2- BC is reported to have significantly higher TROP2 expression than HER2+ BC.

Incidence

Globally, the incidence of HR+/HER2- BC rose from 1.1 million in 2017 to 1.3 million in 2022 and is forecasted to reach 1.5 million in 2030. In China, the incidence of HR+/HER2- BC increased from 173.4 thousand in 2017 to 187.6 thousand in 2022 and is expected to reach 203.8 thousand in 2030.

Treatment Paradigm

Endocrine therapies, such as aromatase inhibitors (AIs) and a selective ER degrader (SERD) represent the cornerstone of standard treatments for advanced HR+/HER2- BC in the U.S. and China. As of the Latest Practicable Date, Trodelvy was the only TROP2 ADC approved for treating advanced HR+/HER2- BC in the U.S., and there was no TROP2 ADC approved for the same indication in China.

In the U.S., the 1L and 2L treatment options for advanced HR+/HER2- BC include various endocrine therapy regimens, such as an AI in combination with a CDK4/6 inhibitor and a SERD with or without a CDK4/6 inhibitor, and combination regimens with an endocrine therapy in combination with either a PI3K inhibitor or a mammalian target of rapamycin inhibitor for patients with PIK3CA mutations. The treatment paradigm in China is similar to that of the U.S. with an additional 2L option containing an AI plus chidamide, an epigenetic modulator.

It is estimated that 40-50% of advanced HR+/HER2- BC patients are resistant to endocrine therapy, who have limited effective treatment options available, leaving a significant unmet need for effective non-endocrine therapy-based treatment.

NSCLC

Lung Cancer (LC) is the second most common cancer and the leading cause of cancer death worldwide. NSCLC is the most common subtype of LC and represents over 85% of all LC cases globally. Approximately 55% of patients with NSCLC have advanced disease at diagnosis. Advanced NSCLC patients have a five-year survival rate of about 8% in the U.S. and less than 5% in China. TROP2 overexpression is reported in about 64% to 75% of patients with NSCLC.

Incidence

The global incidence of NSCLC increased from 1.7 million in 2017 to 2.0 million in 2022 and is expected to grow to about 2.5 million in 2030. In China, the incidence of NSCLC grew from 714.2 thousand in 2017 to 836.8 thousand in 2022 and is anticipated to grow to 1.1 million in 2030.

Treatment Paradigm

The treatment paradigm of advanced NSCLC in the U.S. and China can be broadly classified based on the presence or absence of driver mutations. As of the Latest Practicable Date, there were no TROP2 ADCs approved for NSCLC worldwide.

In the U.S., for driver mutation-positive advanced NSCLC, the 1L treatment options include tyrosine kinase inhibitor (TKI), a type of targeted therapy, directed against specific actionable driver mutations. For driver mutation-negative advanced NSCLC, the 1L+ treatment options include chemoimmunotherapy with or without anti-angiogenic mAb bevacizumab, dual immunotherapy with PD-1 and CTLA-4 inhibitors with or without chemotherapy, and PD-(L)1 inhibitor monotherapy (for PD-L1+ patients).

In China, for driver mutation-positive NSCLC, TKIs are usually considered in the 1L setting. For patients who have failed TKIs, platinum-based doublet chemotherapy with or without bevacizumab, single-agent chemotherapy, or PD-(L)1 inhibitor monotherapy is usually considered. For driver mutation-negative advanced NSCLC, the 1L treatment options include chemoimmunotherapy with or without bevacizumab, doublet chemotherapy with or without PD-(L)1 inhibitor, and monotherapy with a PD-(L)1 inhibitor (for PD-L1+ patients). In the 2L setting, PD-(L)1 inhibitor monotherapy, single-agent chemotherapy and multi-targeting TKI anlotinib (for patients who have failed two chemotherapy regimens) are recommended.

Despite the available treatment options, the prognosis of advanced NSCLC patients remains poor. Although the recent addition of PD-(L)1 inhibitors to standard treatments has improved the survival of patients with driver mutation-negative advanced NSCLC, many patients remain unresponsive. Meanwhile, each TKI is only clinically relevant for a subset of advanced NSCLC patients with a specific driver mutation, with an ORR ranging from approximately 30.0-93.0%. Consequently, there is a significant unmet need for innovative treatments that are potentially effective for a broader patient population regardless of driver mutation status.

GC

GC is the sixth most common and the third most deadly cancer worldwide. The prognosis of GC patients is poor as GC is often diagnosed at an advanced stage. It is estimated that about 40-50% of GC patients have advanced disease at presentation. Advanced GC patients have a five-year survival rate of less than 10% in both the U.S. and China. TROP2 overexpression is reported in about 56% of GC patients.

Incidence

The global incidence of GC increased from 1.0 million in 2017 to 1.2 million in 2022 and is expected to grow to 1.4 million in 2030. China is one of the countries with the highest incidence of GC, accounting for approximately 43.3% of the world's GC patients in 2022. The incidence of GC in China grew from 429.0 thousand in 2017 to 498.6 thousand in 2022 and is anticipated to grow to 619.6 thousand in 2030.

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 PD-1 inhibitors. As of the Latest Practicable Date, there were no TROP2 ADCs approved for GC worldwide.

In the U.S., the 1L treatment options involve combination therapy regimens, including doublet chemotherapy plus HER2 mAb trastuzumab with or without PD-1 inhibitor for advanced HER2+ GC and doublet chemotherapy with PD-1 inhibitor for advanced HER2– GC. Treatments in the 2L+ setting include chemotherapy with or without anti-angiogenic mAb ramucirumab, single-agent chemotherapy and HER2 ADC Enhertu (for HER2+ GC), with combination chemotherapy trifluridine/tipiracil as a 3L+ treatment.

In China, the 1L treatment options involve combination therapy regimens that involve trastuzumab in combination with different chemotherapy for advanced HER2+ GC, doublet or triplet chemotherapy for advanced HER2– GC, and chemoimmunotherapy or PD-1 inhibitor monotherapy for PD-L1+ patients. The 2L treatment options include single-agent chemotherapy, trastuzumab combined with chemotherapy if no prior use of trastuzumab (for HER2+ GC), other chemotherapy regimens not previously used in the 1L and PD-1 inhibitor monotherapy for patients with MSI-high GC. The 3L+ treatment options include HER2 ADC Aidixi, apatinib (an anti-angiogenic TKI), PD-1 inhibitors and single-agent chemotherapy.

There are limited targeted drugs in the existing treatment paradigm of advanced GC and immunotherapy has only modest efficacy. Given that TROP2 is overexpressed in the majority of both HER2+ and HER2– GC patients, ADCs targeting TROP2-expressing tumor cells represent a promising therapeutic strategy to treat a broad GC patient population regardless of HER2 status.

OC

OC is the third most common and the fifth deadliest cancer of the female reproductive system worldwide. About 70% of patients with OC have advanced disease at diagnosis. Advanced OC patients have a five-year survival rate of about 30% in the U.S. and around 30% to 40% in China. TROP2 overexpression is reported in about 59% of OC patients.

Incidence

The global incidence of OC increased from 289.3 thousand in 2017 to 326.4 thousand in 2022 and is expected to reach 379.9 thousand in 2030. The incidence of OC in China grew from 52.0 thousand in 2017 to 57.0 thousand in 2022 and is anticipated to reach 62.4 thousand in 2030.

Treatment Paradigm

Chemotherapy represents the mainstay of standard treatments for advanced OC in the U.S. and China. As of the Latest Practicable Date, there were no ADCs approved for OC worldwide.

The 1L treatments of advanced OC in the U.S. and China primarily involves debulking surgery with various regimens of platinum doublet chemotherapy with or without anti-angiogenic mAb bevacizumab. 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-sensitive OC, platinum doublet chemotherapy, bevacizumab and PARP inhibitors (for patients with deleterious BRCA mutations) are available as the 2L treatment options. For platinum-resistant OC, non-platinum chemotherapy, bevacizumab and PARP inhibitors (for patients with deleterious BRCA mutations) are available as the 2L options. PD-1 inhibitors may be considered for patients with certain immunotherapy biomarkers who have no satisfactory alternative treatment options.

Despite standard treatments, the prognosis of patients with advanced OC remains poor. Given that TROP2 is overexpressed in the majority of OC patients, TROP2 ADCs targeting TROP2-expressing tumor cells represent a promising therapeutic strategy.

Competitive Landscape of the Global TROP2 ADCs Market

As of the Latest Practicable Date, Gilead Sciences' Trodelvy was the only approved TROP2 ADC in the U.S., indicated for advanced TNBC, advanced UC and HR+/HER2- BC, and was the only TROP2 ADC approved by the NMPA for advanced TNBC. As of the same date, there were three TROP2 ADC candidates in phase 2 or beyond globally, including SKB264, Trodelvy (under the drug code of IMMU-132) and DS-1062. The following table illustrates the global competitive landscape of TROP2 ADCs.

Marketed TROP2 ADC Globally

Brand name (Generic name)	Company	Indication	FDA/NMPA approval date	Treatment line	Annual cost (in thousands)	Mono-/Combo-therapy	Country/region	2023 NRDL status	2022 revenue[3] (USD in millions)	2022 Market share[5]
Trodelvy (Sacituzumab govitecan)	Gilead Sciences	Unresectable locally advanced or metastatic TNBC	Apr 2020	3L+	US$372.7[1]	Mono	U.S.	N/A	680[4]	100%
		Locally advanced or metastatic UC	Apr 2021	2L						
		HR+/HER2- BC	Feb 2023	3L+						
		Locally advanced unresectable or metastatic TNBC	Jun 2022	3L+	N/A[2]	Mono	China	No		

Notes:

(1) Assuming the average weight of patients is 80 kg and the duration of treatment is 52 weeks; based on market price in 2023.

(2) Not yet priced in China.

(3) According to the disclosure in 2022 annual report.

(4) Global revenue.

(5) In the global TROP 2 ADC market.

Source: FDA, NMPA, drug label, drug.com, Frost & Sullivan

In 2022, the global revenue of Trodelvy was USD680 million, and it was the only marketed TROP2 ADC globally as of the Latest Practicable Date.

TROP2 ADC Candidates under Clinical Development Globally (phase 2 or beyond)[3]

Drug code (Generic name)	Company[1]	Indication	Clinical stage	First posted date	Mono-/Combo-therapy	Country/region
SKB264	Our Group/MSD	Advanced TNBC	Phase 3	Apr 2022	Mono	China
		TNBC	Phase 2	May 2022	Combo with or without A167	China
		Advanced EGFR-wild type and EGFR-mutant NSCLC (TKI failure)	Phase 2	Jul 2022	Combo with A167 with or without platinum-based chemotherapy	China
		EGFR-mutant NSCLC, NPC (PD-(L)1 relapsed or refractory)	Phase 2	Nov 2022	Mono	China
		Advanced solid tumors (RM-CC, advanced UC, recurrent and metastatic OC, advanced CRPC)	Phase 2	Dec 2022	Combo with Keytruda	China and U.S.
		Advanced EGFR-wild type and EGFR-mutant NSCLC	Phase 2	Mar 2023	Combo with Keytruda, osimertinib and chemotherapy	China
IMMU-132 (Sacituzumab govitecan)	Gilead Sciences	HR+/HER2- BC[2]	Phase 3	Jan 2021	Mono	China
		UC[2]	Phase 3	Jun 2021	Mono	China
		NSCLC	Phase 3	Nov 2022	Combo with Keytruda	U.S.
		PC	Phase 2	Oct 2018	Mono	U.S.
		EC	Phase 2	Jan 2020	Mono	U.S.
		Solid tumor	Phase 2	Nov 2021	Mono	China
		Muscle-invasive Bladder Carcinoma, Stage II and IIIA Bladder Cancer AJCC v8	Phase 2	Oct 2022	Mono	U.S.
		Cervical cancer	Phase 2	May 2023	Mono	U.S.
DS-1062 (Dato-DXd)	Daiichi Sankyo/AstraZeneca	NSCLC	Phase 3	Dec 2020	Mono	Australia, China, EU, Japan, United Kingdom, U.S. etc.
		HR+/HER2- BC	Phase 3	Nov 2021	Mono	China, EU, Japan, United Kingdom, U.S. etc.
		TNBC	Phase 3	May 2022	Mono	China, EU, Japan, United Kingdom, U.S. etc.
		TNBC	Phase 3	Nov 2022	Combo with durvalumab	EU, China, United Kingdom, U.S. etc.
		Advanced/metastatic NSCLC	Phase 3	Jan 2023	Combo with Keytruda, ± chemotherapy	China
		Locally advanced or metastatic NSCLC	Phase 3	Mar 2023	Combo with durvalumab and chemotherapy	China
		Advanced/metastatic solid tumor (EC, GC, metastatic castration-resistant PC, OC, CRC)	Phase 2	Aug 2022	Combo with durvalumab/nivolumab/ bevacizumab/chemotherapy	China, EU, Japan, United Kingdom, U.S. etc.

Notes:

(1) Only companies with drug right are listed.

(2) IMMU-132 was not yet approved for UC or HR+/HER2- BC in China as of the Latest Practicable Date.

(3) From CDE and clinicaltrials.gov.

Source: ClinicalTrials, CDE, Frost & Sullivan

For a competitive advantages analysis of TROP2 ADCs, see "Business – Our Pipeline – Oncology Franchise – ADCs – SKB264 – Competitive Advantages."

CHINA'S HER2 ADC MARKET

Overview

HER2 is a cell surface receptor that is lowly expressed in various normal tissues, but its aberrant activation through overexpression in tumor cells promote their aberrant growth and survival, thus driving the development of various types of cancers including BC and GI cancers such as GC, CRC and esophageal cancer. As a result, HER2 has been a well-established cancer drug target with successful HER2-targeted therapies in different modalities, among which HER2 ADC represents one of the recent and clinically proven strategies.

Addressable Market Size of HER2 ADCs

The table below highlights the major cancers where HER2 is frequently overexpressed. Among them, advanced HER2+ BC, the lead indication of A166, is one of the major types of advanced HER2+ solid tumors. Apart from A166, there were two approved HER2 ADCs, Genentech's Kadcyla and Daiichi Sankyo's Enhertu, and eight HER2 ADCs in phase 2 or beyond, that target the same lead indication as A166 in China as of the Latest Practicable Date. See "– China's HER2 ADC Market – Competitive Landscape of HER2 ADCs" for further details.

Indication	Overexpression[1]
BC	15-30%
GC	10-30%
CRC	3-5%
OC	20-30%
Esophageal Cancer	7-22%
EC	18-80%
NSCLC	13-20%

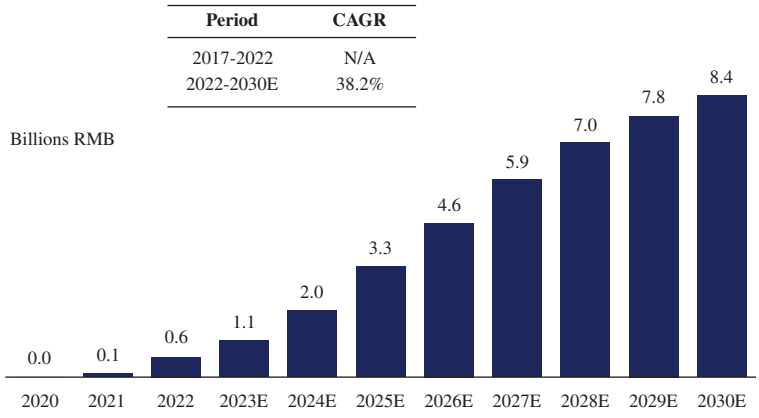
Note:

(1) "Overexpression" refers to the proportion of patients with HER2 overexpression for a given indication.

Sources: Literature Review, Frost & Sullivan

As shown in the charts below, the HER2 ADC market in China was RMB0.6 billion in 2022 and is forecasted to increase to RMB8.4 billion in 2030, representing a CAGR of 38.2% from 2022.

China HER2 ADCs Market Size, 2020-2030E



Sources: NMPA, annual report, MOHRSS, Frost & Sullivan

HER2+ BC

HER2+ BC is a major subtype of BC, representing approximately 15-30% of total BC cases. It is characterized by HER2 overexpression, measured by immunohistochemistry and fluorescence in situ hybridization methods. Compared with HER2– BC, HER2+ BC tends to grow faster and be more aggressive, and patients with HER2+ BC have a worse prognosis. About 20-25% of HER2+ BC patients present with advanced disease at the time of diagnosis, and 20% of early-stage patients eventually develop advanced disease. Patients with advanced HER2+ BC have a five-year survival rate of less than 20% in China.

Incidence

The incidence of HER2+ BC in China increased from 80.1 thousand in 2017 to 86.6 thousand in 2022 and is expected to reach 94.1 thousand in 2030.

Treatment Paradigm

The standard treatments of advanced HER2+ BC in China primarily comprise chemotherapy, targeted therapy such as HER2 mAbs, TKIs and HER2 ADC. As of the Latest Practicable Date, Kadcyla and Enhertu were the only HER2 ADCs approved for advanced HER2+ BC in China.

For advanced HER2+ BC patients eligible for HER2 mAb trastuzumab treatment, 1L treatment options include taxane-based chemotherapy in combination with trastuzumab and pertuzumab, a HER2 dimerization inhibitor, or doublet chemotherapy with trastuzumab. 2L options include combination chemotherapy with a HER2 mAb, or EGFR/HER2 TKI pyrotinib in combination with chemotherapy capecitabine, with triple-combination therapy involving a HER2 mAb pertuzumab or TKIs, and other chemotherapy as the 3L treatment. For advanced HER2+ BC patients who previously failed trastuzumab, pyrotinib in combination with capecitabine is recommended as the 1L treatment. 2L options include HER2 ADC Kadcyla monotherapy and combination therapy with capecitabine and EGFR/HER2 TKI lapatinib. 3L options include EGFR/HER2/HER4 TKI neratinib in combination with capecitabine, pyrotinib monotherapy and other TKI/HER2 mAb-chemotherapy combinations. HER2 ADC Enhertu monotherapy is also approved for patients with unresectable or metastatic HER2+ BC who have received one or more prior anti-HER2-based regimens.

Despite the advances in anti-HER2 therapies, a significant number of patients remain unresponsive or experience treatment resistance and/or significant side effects. Kadcyla and Enhertu, for example, carry notable safety concerns, including black box warning issued by the FDA for hepatic, cardiac and embryo-fetal toxicities for Kadcyla, and interstitial lung disease and embryo-fetal toxicity for Enhertu. These limitations highlight a significant unmet need for safer treatments that can prolong the survival for relapsed or refractory patients.

HER2+ GC

HER2+ GC accounts for about 10-30% of total GC cases. It is characterized by HER2 overexpression, a major actionable oncogenic alteration in GC. About 50% of HER2+ GC patients present with advanced disease at the time of diagnosis. Patients with advanced HER2+ GC have a median OS of 13.8 months in China.

Incidence

The incidence of HER2+ GC in China increased from 102.5 thousand in 2017 to 119.2 thousand in 2022 and is expected to reach 148.1 thousand in 2030.

Treatment Paradigm

The standard treatments of advanced HER2+ GC in China primarily comprise chemotherapy and HER2-directed drugs including HER2 mAb trastuzumab and HER2 ADC Aidixi. As of the Latest Practicable Date, Aidixi was the only HER2 ADC approved for advanced HER2+ GC in China. For details of the standard treatments for advanced HER2+ GC in China, see "– Global and China's TROP2 ADC Markets – Addressable Market Size of TROP2 ADCs – GC – Treatment Paradigm."

Although the use of trastuzumab in combination with chemotherapy in early-line HER2+ GC patients generally improves patient outcome compared with conventional chemotherapy, a significant portion of patients do not respond to trastuzumab and the majority of patients who initially benefit from trastuzumab develop drug resistance. These patients have limited effective 2L+ treatment options, with Aidixi being the only HER2-directed drug available in the 3L+ setting. This underscores a significant unmet need for novel HER2-directed drugs to overcome trastuzumab resistance and widen the treatment options for 2L+ HER2+ GC patients.

HER2+ CRC

CRC is the third most prevalent cancer and a leading cause of cancer mortality in China. HER2+ CRC represents about 3% to 5% of total CRC cases. HER2 overexpression is associated with a more advanced disease stage of CRC. About 36% of patients with HER2+ CRC have advanced disease at diagnosis, and patients with advanced HER2+ CRC have a five-year survival rate of 10% in China.

Incidence

The incidence of HER2+ CRC in China increased from 16.5 thousand in 2017 to 19.3 thousand in 2022 and is expected to reach 24.1 thousand in 2030.

Treatment Paradigm

The treatment paradigm of advanced HER2+ CRC in China largely comprises non-HER2-directed drugs. As of the Latest Practicable Date, there were no ADCs approved for HER2+ CRC in China.

The 1L and 2L treatments for advanced HER2+ CRC largely follow those recommended for advanced CRC with wild-type RAS/BRAF. For patients with certain immunotherapy biomarkers, PD-1 inhibitor is recommended as the 1L treatment. For patients with wild-type RAS/BRAF who can withstand higher treatment toxicity, the 1L treatment includes (i) doublet chemotherapy (5-fluorouracil/leucovorin plus either oxaliplatin (FOLFOX) or irinotecan (FOLFIRI)) with or without EGFR mAb cetuximab (for left-sided tumors), or anti-angiogenic mAb bevacizumab (for right-sided tumors), and (ii) doublet chemotherapy (capecitabine plus oxaliplatin (CAPEOX). For patients who cannot withstand higher treatment toxicity, chemotherapy 5-fluorouracil with or without bevacizumab is recommended as the 1L treatment. For patients who received oxaliplatin in the 1L treatment, FOLFIRI with or without cetuximab or bevacizumab is recommended as the 2L treatment. For patients who received irinotecan in the 1L treatment, 2L treatment options include FOLFOX with or without cetuximab or bevacizumab, and CAPEOX with or without bevacizumab.

As of the Latest Practicable Date, there were no HER2-directed drugs approved by the NMPA for advanced HER2+ CRC. The response rates of advanced HER2+ CRC patients to current non-HER2-directed standard treatments are only between 10.0% to 35.3%, leaving many patients with limited clinical benefit and highlighting the significant unmet need for novel HER2-directed drugs to improve the survival of advanced HER2+ CRC patients. Recent clinical trial results of HER2-directed therapies have demonstrated promising efficacy and favorable safety in HER2+ CRC patients, thus underscoring the potential of HER2-directed therapies for HER2+ CRC.

Competitive Landscape of HER2 ADCs

As of the Latest Practicable Date, Genentech's Kadcyla, Remegen's Aidixi and Daiichi Sankyo's Enhertu were the only three HER2 ADCs approved in China. Kadcyla is indicated for early-stage HER2+ BC and advanced HER2+ BC, Aidixi is indicated for advanced HER2+ GC and advanced HER2+ UC, while Enhertu is indicated for advanced HER2+ BC. As of the same date, there were nine HER2 ADC candidates targeting BC in phase 2 or beyond in China. The following tables illustrate the competitive landscape of HER2 ADCs in China.

Marketed HER2 ADCs in China

Brand name (Generic name)	Company	Indication	NMPA approval date	Treatment line	Annual cost[1] (RMB in thousands)	2023 NRDL status	2022 Revenue[2] (RMB in millions)	2022 Market share[3]
Kadcyla (Ado-trastuzumab emtansine)	Genentech (Roche)	HER2+ early BC	Jan 2020	Adjuvant (post-surgery)	120.0	Yes	N/A	34.4%
		HER2+ unresectable locally advanced/metastatic BC	Jun 2021	2L				
Aidixi (Disitamab vedotin)	RemeGen	HER2 overexpression locally advanced/metastatic GC (including GEJ adenocarcinoma)	Jun 2021	3L	247.0	Yes	N/A	65.6%
		HER2+ locally advanced/metastatic UC	Jan 2022	2L	197.6			
Enhertu (Trastuzumab deruxtecan)	Daiichi Sankyo/ AstraZeneca	HER2+ unresectable or metastatic BC	Feb 2023	2L+	N/A	No	N/A	N/A

Notes:

(1) Assuming the average weight of patients is 60 kg and the duration of treatment is 52 weeks; based on market price in 2023.

(2) According to the disclosure in 2022 annual report.

(3) In China's HER2 ADC market.

Sources: NMPA, drug label, NRDL, Frost & Sullivan

In 2022, according to Frost & Sullivan, Kadcyla and Aidixi had a market share of 34.4% and 65.6%, respectively, among marketed HER2 ADC drugs in China. In the same year, Enhertu was not yet approved.

HER2 ADC Candidates for BC under Clinical Development in China (phase 2 or beyond)

Drug code (Generic name)	Company[1]	Indication	Clinical stage	First posted date
A166	Our Group	Advanced HER2+ BC	NDA registration	Aug 2021
Aidixi (Disitamab Vedotin)	Remegen	HER2+ locally advanced or metastatic BC, HER2+ advanced BC with liver metastasis	Phase 3	May 2018
		HER2 low expression, locally advanced or metastatic BC	Phase 3	May 2020
DS-8201 (Trastuzumab deruxtecan)	Daiichi Sankyo/AstraZeneca	HER2 low expression, HR+ advanced or metastatic BC	Phase 3	Nov 2020
		high risk of HER2+ residual invasive BC	Phase 3	Mar 2021
		HER2+ early BC	Phase 3	Mar 2022
SHR-A1811	Jiangsu Hengrui Medicine	Metastatic BC	Phase 3	Jun 2022
		HER2 low expression recurrent or metastatic BC	Phase 3	Apr 2023
FS-1502	Fosun Pharmaceutical	HER2+ unresectable locally advanced or metastatic BC	Phase 3	Feb 2023
ARX788	Zhejiang Medicine	HER2+ BC	Phase 2/3	Aug 2020
MRG002	Miracogen	HER2+ unresectable locally advanced or metastatic BC	Phase 2/3	May 2021
		HER2 low expression locally advanced or metastatic BC	Phase 2	Feb 2021
		HER2+ BC with liver metastasis	Phase 2	Jan 2022
DX126-262	DAC Biotech Company	HER2+ unresectable locally advanced, or recurrent metastatic BC	Phase 2	Aug 2021
DP303C	CSPC Pharmaceutical Group	HER2+ unresectable locally advanced, recurrent or metastatic BC	Phase 2	Apr 2022

Note:

(1) Only companies with drug right are listed.

Sources: CDE, Frost & Sullivan

For a competitive advantages analysis of HER2 ADCs, see "Business – Our Pipeline – Oncology Franchise – ADCs – A166 – Competitive Advantages."

GLOBAL CLDN18.2 ADC MARKET

Overview

CLDN18.2 is a cell junction protein whose expression is strictly confined to the gastric mucosa, or the innermost layer of the stomach wall, largely inaccessible to targeting antibodies under normal conditions. However, disruptions in cell junctions during cancer development expose CLDN18.2 epitopes on the surface of tumor cells, thus allowing CLDN18.2 to be specifically targeted. Besides GC, CLDN18.2 overexpression has been identified in various types of tumors derived from organs where CLDN18.2 is not normally expressed, such as pancreatic and esophageal cancers. The tumor-selective feature and distribution of CLDN18.2 across some of the most aggressive cancers make CLDN18.2 an attractive candidate for the development of targeted therapy, including novel treatment modalities such as ADCs.

Addressable Market Size of CLDN18.2 ADCs

The table below highlights the major cancers where CLDN18.2 is frequently overexpressed.

Indication	Overexpression[(1)]
PC	60-90%
GC	42-86%
Esophagus adenocarcinoma	30%
Mucinous cystadenoma of ovary	91%

Note:

(1) "Overexpression" refers to the proportion of patients with CLDN18.2 overexpression for a given indication.

Sources: Literature Review, Frost & Sullivan

As of the Latest Practicable Date, there were no CLDN18.2 ADCs approved worldwide. The CLDN18.2 ADC market is directly correlated to and can be estimated by the number of addressable patients with PC and GC, two cancer indications where CLDN18.2 ADCs were more clinically advanced, as of the Latest Practicable Date. Globally, the total addressable patient size of CLDN18.2 ADCs was 1.7 million in 2022 and is forecasted to reach 2.1 million in 2030.

Competitive Landscape of CLDN18.2 ADCs

CLDN18.2 is a relatively new cancer drug target with no CLDN18.2-targeted drugs approved worldwide. As of the Latest Practicable Date, there were 13 CLDN18.2 ADC candidates under clinical development globally, most of which were in early clinical trial stages. The table below summarizes the competitive landscape of CLDN18.2 ADCs globally.

CLDN18.2 ADC Candidates under Clinical Development Globally

Drug code	Company[1]	Indication	Clinical stage	First posted date	Country/region
LM-302	LaNova Medicines	Advanced solid tumor	Phase 1/2	Dec 2021	China
	Turning Point Therapeutics			Aug 2021	U.S.
RC118-ADC	RemeGen	Advanced solid tumor	Phase 1/2	Jan 2022	China
		Unresectable/metastatic/locally advanced solid tumor	Phase 1	Aug 2021	Australia
SHR-A1904	Jiangsu Hengrui Medicine	Advanced solid tumors	Phase 1/2	Mar 2022	Australia, U.S.
		Advanced solid tumors	Phase 1	May 2021	China
		Advanced PC		Jun 2021	
SOT102	SOTIO Biotech	GC, PC, GEJ cancer	Phase 1/2	Sep 2022	Belgium, Czechia, France, Spain, U.S.
CMG901	Keymed Biosciences	Advanced solid tumor, GC, GEJ adenocarcinoma, PC	Phase 1	Mar 2021	China
SYSA1801	CSPC Pharmaceutical Group	Advanced solid tumor, GC, GEJ cancer, PC	Phase 1	Aug 2021	China
CPO102		PC, GC	Phase 1	Sep 2021	N/A
TORL-2-307-ADC	TORL Biotherapeutics	Advanced solid tumor, GC, PC, GEJ adenocarcinoma	Phase 1	Dec 2021	U.S.
SKB315	MSD	Advanced solid tumor	Phase 1	May 2022	China
IBI343	Innovent Biologics	Locally advanced unresectable or metastatic solid tumors	Phase 1	Jul 2022	Australia
JS107	Shanghai Junshi Bioscience	Advanced solid tumor	Phase 1	Aug 2022	China
		Advanced PC		Dec 2022	
ATG-022	Antengene Biologics	Advanced or metastatic solid tumors	Phase 1	Feb 2023	Australia, China
TQB2103	Chia Tai Tianqing Pharmaceutical	Advanced malignant neoplasm	Phase 1	May 2023	China

Note:

(1) Only companies with drug right are listed.

Sources: ClinicalTrials, Frost & Sullivan

For a competitive advantages analysis of CLDN18.2 ADCs, see "Business – Our Pipeline – Oncology Franchise – ADCs – SKB315 – Competitive Advantages."

CHINA'S PD-(L)1 MAB MARKET

Overview of Immune Checkpoint Inhibitors

Cancer immunotherapy has become an integral part of cancer treatment, bringing unprecedented survival benefits to patients with once rapidly fatal cancers by engaging patients' own immune system to fight cancers effectively.

Among the different categories of cancer immunotherapy, immune checkpoint inhibitors represent a core immunotherapeutic approach. Using targeting antibodies to block immune checkpoint proteins, which are negative regulators of T cell activation, immune checkpoint inhibitors counteract immunosuppression exerted by tumor cells and their microenvironment to unleash a powerful antitumor immune response. PD-1, its ligand PD-L1, and CTLA-4 are widely recognized as three of the most clinically validated checkpoint molecules. As of the Latest Practicable Date, all immune checkpoint inhibitors approved globally and in China were in the form of mAbs, except for Kaitanni, a PD-(L)1/CTLA-4 bsAb approved in China. As of the same date, five PD-1 mAbs, three PD-L1 mAbs and two CTLA-4 mAbs were approved by the FDA, while ten PD-1 mAbs, five PD-L1 mAbs and one CTLA-4 mAb were approved in China.

China's PD-(L)1 MAb Market

Overview

PD-1 and its ligand PD-L1 are major immune checkpoint proteins responsible for controlling the continued activation and proliferation of activated T cell effectors. The interaction of PD-1 with PD-L1 can induce T cell exhaustion, a dysfunctional T cell state, to suppress the activity of activated T cells. This immunosuppressive function of PD-(L)1 signaling is often exploited by tumor cells to evade immune attack. Given that PD-1 is widely expressed in immune cells and PD-L1 is overexpressed in many cancers, PD-(L)1 blockade via PD-(L)1 mAbs has clinically proven to be successful in reinvigorating antitumor immune response across a broad range of cancer indications. PD-(L)1 blockade is also associated with a lower incidence of serious AEs compared to chemotherapy and a lower rate of immune-related AEs compared to CTLA-4 blockade. For details of the mechanism of action of PD-(L)1 mAbs, see "Business – Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A167 – Mechanism of Action."

Addressable Market Size of PD-(L)1 MAbs

The PD-(L)1 mAb market in China has grown rapidly since the NMPA approval of the first PD-1 mAb in 2018 and the first PD-L1 mAb in 2019, as PD-(L)1 mAbs have been incorporated into the 1L and 2L treatments for many cancer indications. Expanding cancer indications and the increasing use of combination therapies that couple PD-(L)1 mAbs with other therapeutic agents, such as ADCs, are expected to further expand the PD-(L)1 mAb market in the near future. China's PD-(L)1 mAb market was RMB18.3 billion in 2022 and is anticipated to reach RMB48.3 billion in 2030 at a CAGR of 12.9% from 2022.

TNBC

For details, see "– Global and China's Trop2 ADC Markets – Addressable Market Size of TROP2 ADCs – TNBC."

NSCLC

For details, see "– Global and China's Trop2 ADC Markets – Addressable Market Size of TROP2 ADCs – NSCLC."

NPC

NPC is a type of head and neck cancer that develops in the nasopharynx, an area in the upper part of the throat that connects to the nasal cavities. It has a higher prevalence in China, especially Southern China, than in western countries. RM-NPC represents approximately 35% of total NPC, and patients with RM-NPC have a five-year survival rate of 10-20% in China.

Incidence

The incidence of NPC in China grew from about 59.5 thousand in 2017 to 64.0 thousand in 2022 and is expected to reach 69.1 thousand in 2030.

Treatment Paradigm

For recurrent NPC that cannot be removed by surgery, repeat radiotherapy is the recommended 1L treatment, while the 2L treatment guideline follows that of metastatic NPC. For metastatic NPC, the 1L treatment is combination chemotherapy with or without a PD-1 mAb. The 2L+ treatment options include single-agent chemotherapy and PD-1 mAb monotherapy.

The current standard of care only offers modest therapeutic benefits, with the effective rates of PD-1 mAb monotherapy ranging from approximately 20% to 30%. Given that PD-L1 is expressed in about 89% to 95% of NPC tumors, PD-L1 blockade by PD-L1 mAb is a promising therapeutic strategy to expand the currently limited treatment options for RM-NPC.

Competitive Landscape of PD-(L)1 MAbs Combination Therapies With TROP2 ADCs

As of the Latest Practicable Date, there were five PD-(L)1 mAbs combination therapies with TROP2 ADC in phase 2 or beyond in China.

PD-(L)1 MAbs Combination Therapies With TROP2 ADC Candidates under Clinical Development in China (phase 2 or beyond)

Drug code (Generic name)	Company[(1)]	Indication	Clinical stage	First posted date
A167+SKB264	Our Group	Advanced NSCLC	Phase 2	May 2022
		Advanced TNBC	Phase 2	Jul 2022
Keytruda+SKB264	MSD+Our Group	Solid tumor (r/r CC, LA/metastatic UC, metastatic CRPC, recurrent OC)	Phase 2	Dec 2022
Keytruda+SKB264 +osimertinib+chemotherapy		Advanced EGFR-wild type and EGFR-mutant NSCLC	Phase 2	Mar 2023
Keytruda+DS-1062	MSD+Daiichi Sankyo	Advanced or metastatic NSCLC	Phase 3	Jan 2023
Durvalumab+DS-1062	AstraZeneca+Daiichi Sankyo	Advanced or metastatic solid tumor	Phase 2	Nov 2022
		Locally advanced or metastatic NSCLC	Phase 3	Mar 2023

Note:

(1) Only companies with drug right are listed.

Sources: CDE, Frost & Sullivan

Competitive Landscape of PD-(L)1 MAbs for RM-NPC

As of the Latest Practicable Date, there were three approved PD-1 mAbs and no approved PD-L1 mAbs for treating RM-NPC in China. As of the same date, there were one PD-1 mAb and one PD-L1 mAb at NDA registration stage for RM-NPC in China. The table below sets forth the competitive landscape of PD-(L)1 mAbs for RM-NPC in China.

Marketed PD-1 MAbs for RM-NPC in China

Brand name (Generic name)	Company	Indication	NMPA approval date	Treatment line	Annual cost[(1)] (RMB in thousands)	2023 NRDL status	2022 Revenue[(2)] (RMB in millions)	2022 Market share[(3)]
Tuoyi (Toripalimab)	Shanghai Junshi Biosciences	RM-NPC	Feb 2021	3L+	37.3	Yes	736	4.4%
		Locally RM-NPC	Nov 2021	1L	33.2	No		
Airuika (Camrelizumab)	Jiangsu Hengrui Medicine	Advanced NPC	Apr 2021	3L+	67.0	Yes	3,701.4	20.4%
		Locally RM-NPC	Jun 2021	1L		Yes		
Baizean (Tislelizumab)	Beigene	RM-NPC	Jun 2022	1L	47.8	Yes	2,845.9	16.9%

Notes:

(1) Assuming the average weight of patients is 60 kg and the duration of treatment is 52 weeks; based on market price in 2023.

(2) According to the disclosure in 2022 annual report.

(3) In China's PD-(L)1 mAb market

Source: NMPA, drug label, NRDL, Frost & Sullivan

PD-(L)1 MAb Candidates under Clinical Development for RM-NPC in China (phase 3 or beyond)

Drug code (Generic name)	Company[1]	Indication	Mono/Combo Therapy	Clinical stage	First posted date
AK105/Penpulimab	Akeso Biopharma	Metastatic NPC	Mono	NDA registration	May 2020
		RM-NPC	Combo with Chemotherapy	Phase 3	Jun 2021
A167	Our Group	RM-NPC	Mono	NDA registration	Nov 2021
		RM-NPC	Combo with Chemotherapy	Phase 3	Mar 2022

Note:

(1) Only companies with drug right are listed.

Sources: CDE, Frost & Sullivan

For a competitive advantages analysis of the PD-(L)1 mAbs for treating RM-NPC, see "Business – Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A167 – Competitive Advantages."

CHINA'S EGFR MAB MARKET

Overview

EGFR is a cell surface receptor with key roles in multiple signaling pathways that promote cell proliferation and survival. Aberrant activation of EGFR, such as overexpression or mutation, is widely established as an oncogenic driver in a wide range of cancers, such as CRC, HNSCC and NSCLC. EGFR inhibition has thus become a major focus of targeted therapy with EGFR mAbs being one of the most clinically validated modalities. See "Business – Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A140 – Mechanism of Action" for details regarding the mechanism of action of EGFR mAbs.

In addition to being a promising monotherapy, combining EGFR mAbs with chemotherapy, radiotherapy or chemoradiotherapy has significantly improved patient survival in clinical trials compared to conventional treatments alone.

Addressable Market Size of EGFR mAbs

The EGFR mAb market in China grew from RMB0.8 billion in 2017 to RMB4.1 billion in 2022 at a CAGR of 37.3%. With the anticipated biosimilars market entry and new EGFR mAb launches, China's EGFR mAb market is expected to reach RMB10.6 billion in 2030, representing a CAGR of 12.8% from 2022.

RAS wild-type mCRC

CRC is the third most prevalent type of cancer in China. About 20% of patients with CRC have metastases at the time of diagnosis, and around 80% of patients with CRC develop metastatic disease. The overall five-year survival rate for mCRC is only around 10%. RAS wild-type mCRC, a major type of mCRC targetable by EGFR-directed therapies, represents approximately half of all mCRC cases.

Incidence

The incidence of RAS wild-type mCRC in China grew from 173.7 thousand in 2017 to 202.5 thousand in 2022 and is expected to reach 253.6 thousand in 2030.

Treatment Paradigm for RAS Wild-type mCRC

In China, the treatment paradigm for RAS wild-type mCRC primarily involves combination chemotherapy with cetuximab or anti-angiogenic mAb bevacizumab. For details regarding the standard treatments for RAS wild-type mCRC, see "– China's HER2 ADC Market – Addressable Market Size of HER2 ADCs – HER2+ CRC – Treatment Paradigm."

HNSCC

HNSCC is a group of cancers arising from mucosal surfaces of the mouth, nose and throat and accounts for more than 90% of head and neck cancer. Locally advanced HNSCC (LA-HNSCC) accounts for approximately 60% of all HNSCC cases, and RM-HNSCC accounts for approximately 50% of all HNSCC cases. The five-year survival rate of patients with LA-HNSCC and RM-HNSCC in China is 50% and 3.6%, respectively.

Incidence

The incidence of LA-HNSCC in China grew from about 72.4 thousand in 2017 to 80.5 thousand in 2022 and is expected to reach 91.9 thousand in 2030. The incidence of RM-HNSCC in China grew from about 60.3 thousand in 2017 to 67.1 thousand in 2022 and is expected to reach 76.6 thousand in 2030.

Treatment Paradigm

For LA-HNSCC, the current treatment paradigm in China consists of surgery, radiotherapy, platinum-based chemotherapy and targeted therapy. 1L treatment options include surgery with or without radiotherapy or radiochemotherapy, radiotherapy in combination with platinum-based chemotherapy, and induction chemotherapy followed by radiotherapy, with cetuximab in combination with radiotherapy available in the 2L setting.

For RM-HNSCC, palliative platinum-based chemotherapy with or without targeted therapy is currently the mainstay of treatment for patients not suitable for surgery and radiotherapy. In China, PD-1 mAb monotherapy and doublet chemotherapy in combination with cetuximab represent the 1L treatment options, with PD-1 inhibitor nivolumab as monotherapy in the 2L setting.

Competitive Landscape of EGFR mAbs

As of the Latest Practicable Date, two EGFR mAbs, cetuximab and nimotuzumab, were approved in China.

Marketed EGFR MAbs in China

Brand name (Generic name)	Company	Indication	NMPA approval date	Treatment line	Annual cost[1] (RMB in thousands)	2023 NRDL status	2022 Revenue[2] (RMB in millions)	2022 Market share[3]
Theraloc (Nimotuzumab)	Biotech Pharma	NPC	Jan 2008	1L	23.0	Yes	N/A	40.6%
Erbitux (Cetuximab)	Eli Lilly and Company, Merck, BMS	RAS wild-type mCRC	Sep 2019	1L	137.8	Yes	N/A	59.4%
		RM-HNSCC	Mar 2020					
		LA-HNSCC	Jun 2022			Yes		

Notes:

(1) Assuming the average weight of patients is 60 kg and the duration of treatment is 52 weeks; based on market price in 2023.

(2) According to the disclosure in 2022 annual report.

(3) In China's EGFR mAb market.

Source: NMPA, drug label, NRDL, Frost & Sullivan

China's clinical development landscape for EGFR mAbs is dominated by cetuximab biosimilars, mainly driven by superior market performance of cetuximab and expiration of patent protection for cetuximab in China in 2017, opening the door for biosimilars to enter the market. As of the Latest Practicable Date, no cetuximab biosimilars had been approved by the NMPA, and there were two cetuximab biosimilar candidates in phase 3 or beyond in China. The following table sets forth the competitive landscape for cetuximab biosimilars in China.

Cetuximab Biosimilar Candidates under Clinical Development in China (phase 3 or beyond)

Drug code	Company[(1)]	Indication	Clinical stage	First posted date
APZ001	ANNPO Biotechnology	mCRC	Phase 3	Oct 2019
A140	Our Group	RAS wild-type mCRC	Phase 3	Dec 2020

Note:

(1) Only companies with drug right are listed.

Sources: CDE, Frost & Sullivan

For a competitive advantages analysis of cetuximab biosimilar candidates, see "Business – Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A140 – Competitive Advantages."

CHINA'S SELECTIVE RET INHIBITOR MARKET

Overview

Rearranged during transfection (RET) gene is a cell surface signaling receptor that regulates cell differentiation, growth and migration. Genetic alterations of RET, such as mutations and fusions, have been implicated in the pathogenesis of approximately 2% of human cancers ("RET+ cancers"), including about 1-2% of NSCLC and 33% of thyroid cancer (TC). Selectively inhibiting RET has thus been a promising approach to treat RET+ cancers. See "Business – Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A400 – Mechanism of Action" for details of the mechanism of action of selective RET inhibitors.

Addressable Market Size of Selective RET Inhibitors

Following the NMPA approval of the first selective RET inhibitor in 2021, the selective RET inhibitor market in China is expected to increase from RMB0.3 billion in 2022 to RMB1.8 billion in 2030 at a CAGR of 22.9% from 2022.

RET+ NSCLC

RET+ NSCLC amounts to approximately 1% to 2% of total NSCLC cases. See "– Global and China's TROP2 ADC markets – Addressable Market Size of TROP2 ADCs – NSCLC" for details regarding NSCLC.

Incidence

The incidence of RET+ NSCLC in China grew from 13.6 thousand in 2017 to 15.9 thousand in 2022 and is expected to reach 20.0 thousand in 2030.

Treatment Paradigm

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

Standard non-RET inhibitor therapies provide limited benefit for RET+ NSCLC patients, and the therapy outcomes in these patients are generally poor. Although two selective RET inhibitors, Gavreto and Retevmo, have been added to the standard treatments, their therapeutic benefits are limited by acquired resistance partially due to RET mutations developed during the treatment course, as well as safety issues such as hypertension and hematological toxicity, necessitating the development of novel selective RET inhibitors with improved safety and better efficacy against drug resistant mutations.

RET+ MTC

TC is a type of cancer that develops in the thyroid gland. It has been among the fastest growing cancers in China in recent years. Medullary TC (MTC) is one of the subtypes of TC, accounting for about 3% of total TC cases. RET mutations represent a major driver of MTC. They occur in about 90% of MTCs and are associated with advanced disease and a poor clinical outcome.

Incidence

The incidence of RET+ MTC in China grew from 5.6 thousand in 2017 to 6.2 thousand in 2022 and is expected to reach 7.4 thousand in 2030.

Treatment Paradigm

The treatment paradigm of advanced unresectable RET+ MTC in China includes selective RET inhibitor Gavreto in the 1L setting and selective RET inhibitor Retevmo in the 2L setting. Despite the initially promising treatment responses to Gavreto and Retevmo, many patients eventually progress as their tumors acquire RET resistant mutations to these two selective RET inhibitors. Moreover, Retevmo and Gavreto are associated with safety issues such as hypertension and hematological toxicity that limit their clinical use. This indicates a significant unmet need for novel selective RET inhibitors with improved safety and better efficacy against drug resistant mutations.

Competitive Landscape of Selective RET Inhibitors

As of the Latest Practicable Date, Gavreto and Retevmo were the only two selective RET inhibitors approved in China, and there were six selective RET inhibitor candidates in phase 1/2 or beyond in China as of the same date.

Marketed Selective RET Inhibitors in China

Brand name (Generic name)	Company	Indication	NMPA approval date	Treatment line	Annual cost[1] (RMB in thousands)	2023 NRDL status	2022 Revenue[2] (RMB in millions)	2022 Market share[3]
Gavreto (Pralsetinib)	CStone Pharmaceuticals	Metastatic RET fusion-positive NSCLC	Mar 2021	2L	728.0	No	N/A	100%
		Advanced or metastatic RET fusion-positive TC	Mar 2022	1L				
		Advanced or metastatic RET-mutant MTC						
Retevmo (Selpercatinib)	Eli Lilly and Company	Metastatic RET fusion-positive NSCLC	Oct 2022	1L	1,855.9	No	N/A	N/A
		Adults with advanced or metastatic RET mutated MTC						
		Advanced or metastatic RET fusion positive TC						

Notes:

(1) Assuming the average weight of patients is 60 kg and the duration of treatment is 52 weeks; based on market price in 2023.

(2) According to the disclosure in 2022 annual report.

(3) In China's selective RET inhibitor market.

Source: NMPA, drug label, NRDL, Frost & Sullivan

Selective RET Inhibitor Candidates under Clinical Development in China (phase 1/2 or beyond)

Drug code (Generic name)	Company[1]	Indication	Clinical stage	First posted date
Loxo-292 (Selpercatinib)	Eli Lilly	RET fusion solid tumor, RET mutant MTC and other RET active tumor	Phase 2	Jan 2020
BYS10	Baiyunshan Pharmaceutical	Adult advanced solid tumor	Phase 1/2	Apr 2022
Blu-667	CStone Pharmaceuticals	Adult MTC, RET fusion NSCLC and other RET mutant advanced solid tumor	Phase 1/2	May 2019
A400	Our Group	Advanced RET+ solid tumor	Phase 1/2	Jul 2021
HEC169096	Sunshine Lake Pharma	NSCLC, MTC and other solid tumors	Phase 1/2	Jun 2022
TY-1091	TYK Medicines	NSCLC, MTC and other advanced solid tumors	Phase 1/2	Dec 2022

Note:

(1) Only companies with drug right are listed.

Sources: CDE, Frost & Sullivan

For a competitive advantages analysis of selective RET inhibitors, see "Business – Our Pipeline – Oncology Franchise – Other Modalities (Immunotherapies and Targeted Therapies) – A400 – Competitive Advantages."

CHINA'S JAK INHIBITOR MARKET

Overview

Janus kinases (JAKs) are key enzymes responsible for transducing cytokine signals via the JAK-STAT pathway, which is a common pathway for many cytokines to modulate immune response and for the development of blood cells. However, due to its central role in mediating immune-related signals, dysregulation of the JAK-STAT pathway is implicated in a wide range of diseases, including autoimmune diseases such as rheumatoid arthritis (RA) and alopecia areata (AA), as well as hematological cancers. Blocking the JAK-STAT pathway using JAK inhibitors is a promising approach for treating a broad range of indications, clinically validated by the approval of several JAK inhibitors for treating multiple autoimmune diseases and certain hematological cancers. See "Business – Our Pipeline – Non-Oncology Franchise – A223 – Mechanism of Action" for details regarding the mechanism of action of JAK inhibitors in RA and AA.

Addressable Market Size of JAK Inhibitors

The JAK inhibitor market in China grew from RMB0.1 billion in 2017 to RMB2.0 billion in 2022 at a CAGR of 80.9%. Driven by an increasing addressable patient population, potential indication expansion and the anticipated market entry of novel JAK inhibitors, China's JAK inhibitor market is projected to expand rapidly in the near future, reaching RMB22.1 billion in 2030 at a CAGR of 35.1%.

RA

RA is a prevalent chronic systemic autoimmune disease. It is characterized by chronic inflammation in the joints that gradually damages joint tissues as the disease progresses, leading to potentially debilitating symptoms including joint stiffness, pain and swelling that compromise patients' quality of life.

Prevalence

RA affects a large population in China. The prevalence of RA in China increased from 5.8 million in 2017 to 6.0 million in 2022, and is expected to reach 6.2 million in 2030.

Treatment Paradigm

There is currently no cure for RA. The management of RA in China aims to achieve low disease activity or remission and to control joint damage and pain via long-term use of disease-modifying anti-rheumatic drugs (DMARDs). Currently, the 1L treatment for RA is conventional synthetic DMARD (csDMARD) monotherapy with methotrexate (MTX) recommended as the first choice when it is not contraindicated. The 2L treatment options include the addition of either a biologic DMARD (bDMARD) such as a TNF inhibitor, or a JAK inhibitor to the csDMARD.

Compared to bDMARDs that target individual cytokines, JAK inhibitors can simultaneously interrupt the downstream signaling of multiple cytokines, which potentially underlies their effectiveness in RA patients who have failed multiple csDMARDs/bDMARDs therapies. Moreover, bDMARDs are large proteins that may cause immunogenicity, i.e., evoking an undesirable immune response, and require either intravenous infusion or subcutaneous injection for dosing. Conversely, JAK inhibitors are small molecules that are non-immunogenic and can be administered orally, thus potentially improving ease of dosing and treatment compliance. However, the approved JAK inhibitors have major safety issues, with black box warning issued by the FDA for increased risks of serious side effects including serious infection, death, malignancy, thrombosis, and major adverse cardiovascular events. This underscores a significant unmet need for novel JAK inhibitors with improved safety profile.

AA

AA is a common, distressing autoimmune disease characterized by transient, non-scarring hair loss due to an abnormal immune system that attacks hair follicles. Patients with AA tend to have a variable, relapsing-remitting disease course with multiple episodes of hair loss.

Prevalence

AA affects a large population in China with a rising prevalence. The prevalence of AA in China grew from 3.5 million in 2017 to 4.0 million in 2022 and is projected to reach 4.5 million in 2030.

Treatment Paradigm

In China, treatment options for AA are limited with only Minoxidil, a potassium channel opener, and Olumiant approved as the only disease-specific treatments for severe AA. Inhibiting JAK1/2 represents a clinically proven strategy for AA, underlined by the FDA approval of Olumiant (baricitinib) as the first and only systemic treatment for severe AA and its recent NMPA approval for the same indication.

Competitive Landscape of JAK Inhibitors

As of the Latest Practicable Date, there were three JAK inhibitors approved by the NMPA for treating RA and seven JAK inhibitor candidates in phase 2 or beyond for treating the same indication in China. The JAK inhibitor market for treating AA is emerging with Olumiant recently approved in March 2023 and four JAK inhibitor candidates, in phase 2 or beyond as of the Latest Practicable Date. The following tables summarize the competitive landscape of JAK inhibitors in China.

Marketed Selective JAK Inhibitors in China

Brand name (Generic name)	Company	Targets	Indication	NMPA approval date	Treatment line	2023 NRDL status	2022 Revenue[1] (RMB in millions)	2022 Market share[2]
Xeljanz (Tofacitinib)	Pfizer	JAK1	RA	Mar 2017	2L	Yes	N/A	6.0%
			Ankylosing spondylitis	Apr 2022	2L/3L			
			Psoriatic arthritis	Oct 2022	1L			
Jakafi (Ruxolitinib)	Novartis	JAK1, JAK2	Myelofibrosis	Mar 2017	2L	Yes	N/A	42.3%
			Graft-versus-host disease	Mar 2023	2L	No		
Olumiant (Baricitinib)	Eli Lilly and Company	JAK1, JAK2	RA	Jun 2019	–	Yes	N/A	11.6%
			AA	Mar 2023	–	No		
Rinvoq (Upadacitinib)	AbbVie	JAK1	Atopic dermatitis	Feb 2022	2L	Yes	N/A	0.1%
			RA	Mar 2022	2L			
			Psoriatic arthritis	Apr 2022	2L			
			Ulcerative colitis	Feb 2023	N/A	No		
Cibinqo (Abrocitinib)	Pfizer	JAK1	Atopic dermatitis	Apr 2022	–	Yes	N/A	0.3%

Notes:

(1) According to the disclosure in 2022 annual report.

(2) In China's JAK inhibitor market.

Sources: NMPA, drug label, NRDL, Frost & Sullivan

JAK Inhibitor Candidates for RA and AA under Clinical Development in China (phase 2 or beyond)

Drug code	Company	Indication	Clinical stage	First posted date
ASP015K (peficitinib)	Astellas Pharma	RA	NDA registration	Jul 2018
PF-06651600 (ritlecitinib)	Pfizer	AA	NDA registration	Jun 2019
Jaktinib	Zelgen Biopharmaceuticals	Moderate-to-severe AA	Phase 3	Jun 2021
SHR0302	Jiangsu Hengrui Medicine	Moderate-to-severe RA	Phase 3	May 2020
		Severe adult AA	Phase 3	Jan 2022
LW402	Longwood Biopharmaceuticals	Moderate-to-severe RA	Phase 2	Nov 2022
A223	Our Group	Moderate-to-severe RA	Phase 2	Dec 2020
		Severe AA	Phase 2	Aug 2022
WXFL10203614	Wuxi Fortune Pharmaceutical	Moderate-to-severe RA	Phase 2	Dec 2020
LNK01001	Lynk Pharmaceuticals	Moderate-to-severe RA	Phase 2	Sep 2021
TLL-018	GaoLing Pharmaceutical Company	RA	Phase 2	Nov 2021

Sources: CDE, Frost & Sullivan

For a competitive advantages analysis of the JAK inhibitor candidates, see "Business – Our Pipeline – Non-Oncology Franchise – A223 – Competitive Advantages."

REPORT COMMISSIONED BY FROST AND SULLIVAN

In connection with the [**REDACTED**], we have engaged Frost & Sullivan to conduct a detailed analysis and prepare an industry report on the major markets for which our drug candidates are positioned. Frost & Sullivan is an independent global market research and consulting company which was founded in 1961 and is based in the United States. We have agreed to pay Frost & Sullivan a total fee of RMB0.88 million for the preparation of the Frost & Sullivan 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 Frost & Sullivan Report. Except for the Frost & Sullivan Report, we did not commission any other industry report in connection with the [**REDACTED**].

We have included certain information from the Frost & Sullivan Report in this document because we believe such information facilitates an understanding of the pharmaceutical market for potential [**REDACTED**]. Frost & Sullivan prepared its report based on its in-house database, independent third-party reports and publicly available data from reputable industry organizations. Where necessary, Frost & Sullivan contacts companies operating in the industry to gather and synthesize information in relation to the market, prices and other relevant information. Frost & Sullivan believes that the basic assumptions used in preparing the Frost & Sullivan Report, including those used to make future projections, are factual, correct and not misleading. Frost & Sullivan has independently analyzed the information, but the accuracy of the conclusions of its review largely relies on the accuracy of the information collected. Frost & Sullivan research may be affected by the accuracy of these assumptions and the choice of these primary and secondary sources.