The information and statistics set out in this section and other sections of this document were extracted from the report prepared by Frost & Sullivan, which was commissioned by us, and from various official government publications and other publicly available publications. 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 Sole Sponsor, the* [**REDACTED**], *the* [**REDACTED**], *the* [**REDACTED**], *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, fairness and completeness.*

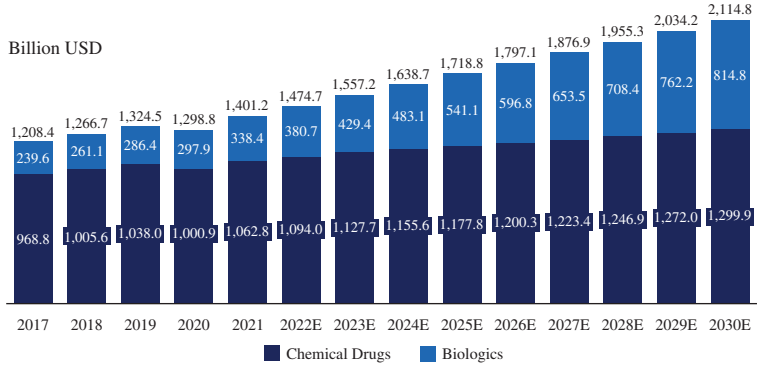
GLOBAL AND CHINA PHARMACEUTICAL MARKET

Overview

The global pharmaceutical market is comprised of two segments, namely chemical drugs and biologics. As illustrated in the chart below, from 2017 to 2021, the size of the global pharmaceutical market experienced an increase from US$1,208.4 billion to US$1,401.2 billion, representing a CAGR of 3.8%. The size of the global pharmaceutical market is expected to continue growing in the near future and is forecasted to reach US$1,718.8 billion and US$2,114.8 billion in 2025 and 2030, respectively, representing a CAGR of 5.2% from 2021 to 2025 and 4.2% from 2025 to 2030.

Global Pharmaceutical Market, 2017-2030E

Period	CAGR		
	Chemical Drugs	Biologics	Total
2017-2021	2.3%	9.0%	3.8%
2021-2025E	2.6%	12.4%	5.2%
2025E-2030E	2.0%	8.5%	4.2%

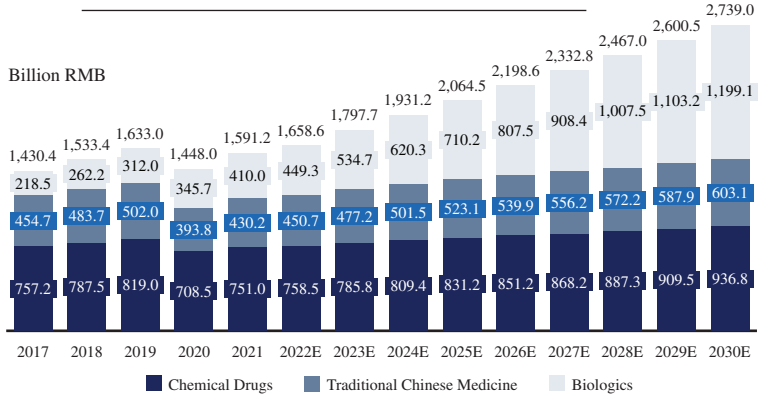


Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, Frost & Sullivan Analysis

China's pharmaceutical market, on the other hand, is comprised of chemical drugs, traditional Chinese medicine (TCM) and biologics. In line with the growth of the global pharmaceutical market and propelled by the economy growth and demand for healthcare in China, the size of the China pharmaceutical market increased from RMB1,430.4 billion in 2017 to RMB1,591.2 billion in 2021, representing a CAGR of 2.7%. The size of the China pharmaceutical market is projected to grow at a slightly faster pace than that of the global pharmaceutical market to reach RMB2,064.5 billion in 2025 and RMB2,739.0 billion in 2030, representing a CAGR of 6.7% from 2021 to 2025 and 5.8% from 2025 to 2030.

China Pharmaceutical Market, 2017-2030E

Period	CAGR			
	Chemical Drugs	TCM	Biologics	Total
2017-2021	-0.2%	-1.4%	17.0%	2.7%
2021-2025E	2.6%	5.0%	14.7%	6.7%
2025E-2030E	2.4%	2.9%	11.0%	5.8%



Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, Frost & Sullivan Analysis

GLOBAL AND CHINA ONCOLOGY DRUG MARKET

Overview

Cancer is a broad group of diseases in which cells divide and grow in an uncontrolled fashion and which are usually classified as either hematological malignancies or solid tumors. It is the leading cause of death worldwide and is rapidly overtaking heart disease in many countries to become the number one cause of mortality. Oncology treatments have undergone significant development over the years, with chemotherapeutic drugs, targeted therapy and immune-oncology therapy becoming the major oncology treatments available to date. Chemotherapeutic drugs are the first systemic drugs to treat cancer. Although widely used in a broad range of indications, they frequently cause severe side effects. Since the early 2000s, there has been major progress in developing targeted small molecule drugs and mAbs, which have revolutionized oncology treatments, and many of them have become global blockbuster drugs. In recent years, BsAbs have attracted increasing interest in scientific and clinical research as a next-generation antibody therapy approach for the treatment of cancer. Through binding to two different antigen sites, BsAbs are able to provide robust and more specific targeting.

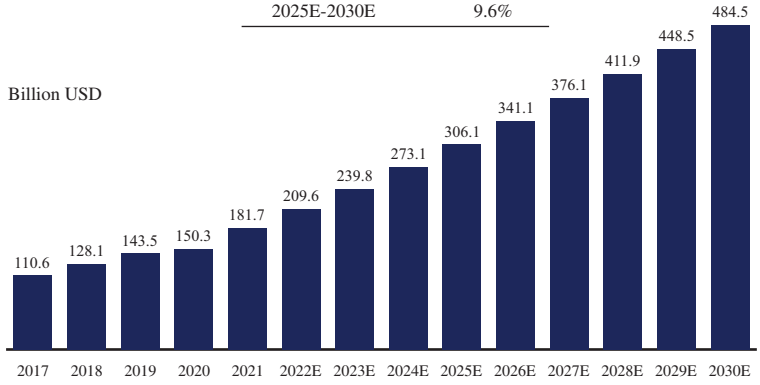
The global and China oncology drug markets are fiercely competitive in terms of the number, modalities and expected clinical performance of currently available treatments. Major modalities of oncology therapy include chemotherapy, targeted therapies, immune checkpoint inhibitor (ICI) mAbs, cell and gene therapies (CGT), and BsAbs. Currently, there are approximately a thousand chemotherapy drugs available globally and in China for cancer treatment. For example, with respect to HER2-targeted therapies, there are currently 23 approved antibody drugs worldwide, and over 500 antibody pipelines are in the clinical phase globally. For ICI mAbs, taking anti-PD-1 mAbs as an example, there are currently 16 approved drugs globally, and over 200 pipelines are in the clinical phase. Globally, there are 6 approved cell therapy products (excluding genetically modified products) and 14 approved gene therapy products for the treatment of cancer. Many approved oncology drugs and drug candidates under clinical development have demonstrated encouraging clinical efficacy and safety profile in cancer treatment.

Compared to chemotherapy, BsAbs offer a targeted and immune-mediated approach with higher effectiveness, specificity, and fewer side effects. BsAbs and ICI mAbs both harness the immune system, but BsAbs have a higher specificity. When compared to CGT, BsAbs exhibit a similar high level of specificity and effectiveness, yet have fewer side effects and are less costly.

As illustrated in the chart below, from 2017 to 2021, the size of the global oncology drug market experienced a significant increase from US$110.6 billion to US$181.7 billion, representing a CAGR of 13.2%. The size of the global oncology drug market is expected to continue growing in the near future and is forecasted to reach US$306.1 billion and US$484.5 billion in 2025 and 2030, respectively, representing a CAGR of 13.9 % from 2021 to 2025 and 9.6% from 2025 to 2030.

Global Oncology Drug Market, 2017-2030E

Period	CAGR
2017-2021	13.2%
2021-2025E	13.9%
2025E-2030E	9.6%

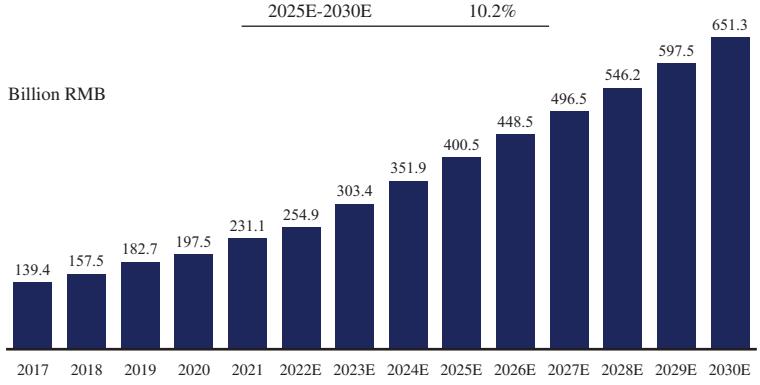


Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, IARC, GLOBOCAN, Frost & Sullivan Analysis

Consistent with the growth of the global oncology drug market and driven by the steady rise of sales of oncology products in China in recent years, the size of the China oncology drug market increased from RMB139.4 billion in 2017 to RMB231.1 billion in 2021, representing a CAGR of 13.5%. The size of the China oncology drug market is projected to grow at a slightly faster pace than that of the global oncology drug market to reach RMB400.5 billion in 2025 and RMB651.3 billion in 2030, representing a CAGR of 14.7% from 2021 to 2025 and 10.2% from 2025 to 2030.

China Oncology Drug Market, 2017-2030E

Period	CAGR
2017-2021	13.5%
2021-2025E	14.7%
2025E-2030E	10.2%

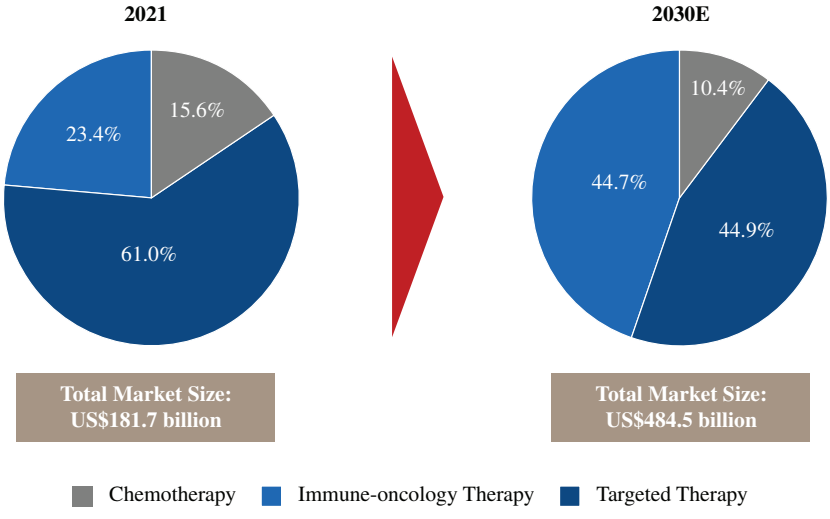


Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, NCCR, Frost & Sullivan Analysis

Global and China Oncology Market by Therapy

According to Frost & Sullivan, the global oncology market was dominated by targeted therapy, which took up to approximately 61.0% of the global market in 2021. In 2030, targeted therapy and the immune-oncology therapy are expected to account for 44.9% and 44.7% of the global oncology market, representing an aggregate market size of US$217.5 billion and US$216.6 billion, respectively.

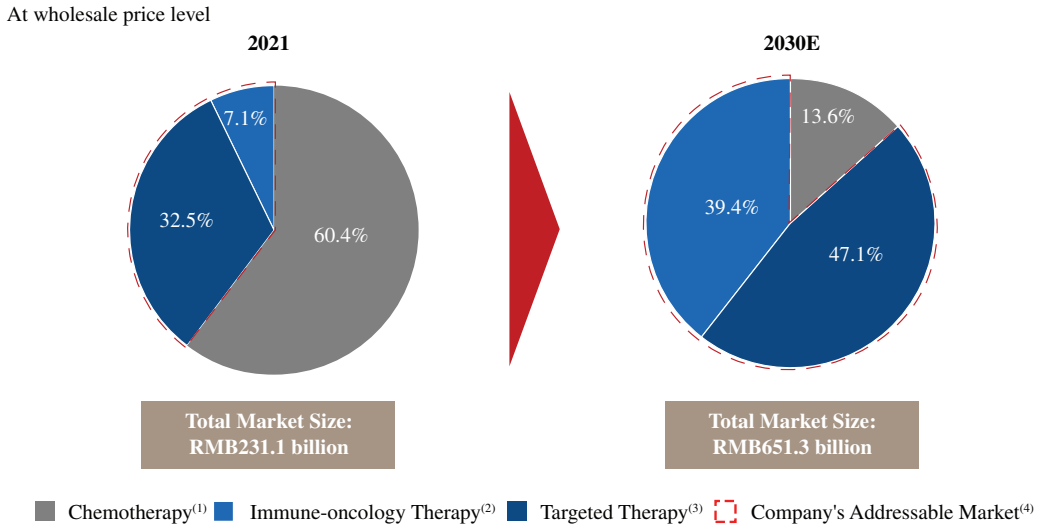
Breakdown of Global Oncology Market by Therapy, 2021 and 2030E



Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, IARC, GLOBOCAN, Frost & Sullivan Analysis

In contrast, China's oncology market in 2021 was dominated by chemotherapy drugs, which took up to approximately 60.4% of the total market. According to Frost & Sullivan, due to factors such as reimbursement policies, new drug developments and patients' increasing affordability, targeted therapy and immune-oncology therapy are expected to occupy most of the market by 2030, with market share of 47.1% and 39.4% of China's oncology market, respectively, representing an aggregate market size of approximately RMB306.8 billion and RMB256.6 billion, respectively.

Breakdown of China Oncology Market by Therapy, 2021 and 2030E



Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, NCCR, Frost & Sullivan Analysis

Notes:

(1) Chemotherapy is the use of medicines or drugs to inhibit cell proliferation and tumor multiplication, thereby avoiding invasion and metastasis. These medicines may require repetition to achieve a response and do not differentiate between cancerous cells and healthy cells.

(2) Immune-oncology therapy enhances or restores the immune system's ability to detect and destroy cancer cells by overcoming the mechanisms by which tumors evade and suppress immune responses. Immune-oncology therapy functions through several approaches such as activating the immune system in a cytokine-dependent manner, manipulating the feedback mechanisms involved in the immune response, and enhancing the immune response via lymphocyte expansion. These techniques can be used as monotherapies or combination therapies. Common immune-oncology therapy approaches include the use of cytokines (e.g. anti-TGF-β), adoptive cell transfer, vaccines, and antibodies targeting immune checkpoints (e.g. anti PD-L1) and/or other T subsets (e.g. anti-CD3).

(3) Targeted therapy is a type of precise cancer treatment that controls the growth, division, and metastasis of tumors through blocking essential biochemical pathways or mutant proteins that are required for tumor cell growth and survival, and has been widely utilized and proven effective in many types of solid tumors. Targeted therapy can inhibit tumor progression and induce striking regressions in molecularly defined subsets of patients. Normally, targeted therapy involves the use of antibodies or oral small drugs. Antibodies block specific targets either on the outside of cancer cells or in the tissue surrounding it (e.g. CD38, EpCAM, ANG2). Oral small drugs are smaller chemical components than monoclonal antibodies, which allows cells to absorb them better, so that they could bind to the intracellular targets (e.g. EGFR-TKI, VEGF, HER2).

(4) As of the Latest Practicable Date, six of the Company's seven pipeline drug candidates were BsAbs designed as either immune-oncology therapy or targeted therapy. Although immune-oncology therapy and targeted therapy are both specific methods for cancer treatment, there are some features that distinguish them from each other. Immune-oncology therapies typically enhance or restore the immune system's ability to detect and destroy cancer cells, and targeted therapies usually eliminate tumors by blocking targets engaged in essential biochemical pathways that are required for tumor cell growth and survival. BsAbs can simultaneously target two antigens or epitopes, and this dual function enables them to simultaneously regulate immunological reactions and interfere with the essential signal pathways for tumor metastasis. These characteristics make BsAbs difficult to accurately identify as either immune-oncology therapy or targeted therapy. Consequently, while the Company's seven BsAb drug candidates can address both immune-oncology therapy and targeted therapy markets, it is difficult to precisely categorize each of the Company's BsAb drug candidates.

Growth Drivers and Future Trends of China Oncology Drug Market

The key growth drivers of China's oncology drug market include: (a) the increasing patient pool; (b) the medical needs due to the limited number of available oncology therapies compared to the global market; (c) the improving affordability; (d) the favorable regulatory policies issued by the Chinese government in facilitating the review for, and in encouraging the development of, innovative drugs, including the Reform of Review and Approval System for Drugs and Medical Devices to Encourage Innovation (the Opinion) (《關於深化審評審批制度改革鼓勵藥品醫療器械創新的意見》) promulgated by the CFDA in January 2018, which promotes the integration of drug registration technical standards with international standards, accelerate the drug examination and approval process, and strengthening the management for the life cycle of drugs, including BsAbs; and (e) the emergence of combination therapies which is expected to further enrich the availability of oncology therapies and drive the growth of the oncology drug market.

The future trends of China's oncology drug market mainly include: (a) the promotion of precision treatment, as innovative targeted drugs are continuously explored, precision treatment of cancer will be applied to wider tumor-related targets; (b) wider use of combination therapies, as continuous attempts are being made to involve new drugs and new combinations such as Chimeric Antigen Receptor T-Cell Immunotherapy (CAR-T) with chemotherapy and other mAbs, which will further encourage and expediate potential effective combinations to be applied in clinical practices more extensively; (c) managing cancer as a chronic disease with the development of new treatments which extend the survival period of cancer patients; and (d) the introduction of favorable regulatory policies which will accelerate the review and approval of new drugs, and the inclusion of a variety of anti-tumor drugs in the new medical insurance catalog which greatly reduces patients' economic burden.

GLOBAL AND CHINA ANTIBODY DRUG MARKET

Overview

Over the past decade, antibody engineering has evolved dramatically. As a result, therapeutic antibodies have become the predominant treatment modality for various diseases in recent years, and also among the best-selling drugs in the global pharmaceutical market. Antibody drugs are the largest category of therapeutic biologics, which have generally shown higher efficacy and lower toxicity in treating cancers than traditional therapies such as chemotherapy and radiotherapy. Antibodies target tumor-selective antigens with a high degree of target specificity, which reduces off-target toxicity and side effects, and have gained increasing acceptance among patients and doctors.

According to Frost & Sullivan, antibody drugs include mAbs, BsAbs, antibody-drug conjugate (also known as conjugated monoclonal antibodies), and multi-specific antibodies. The following table sets forth the classification and comparative analysis of therapeutic antibody drugs:

Categories	Structure and Functions	Advantages	Limitations	Entry Barriers	Future Trends
Monoclonal antibody (mAb)	Monoclonal antibodies are made by identical immune cells that are from a unique parent cell. mAb can have bivalent affinity, in that they bind to the same antigenic determinant.	Proven therapeutic effect for several kinds of diseases, especially for cancers and autoimmune diseases. High homogeneity. Possibility to produce large quantities of identical antibody.	Diffuse poorly and large tumor masses may be more difficult to treat by mAb therapy. Triggering antibody-dependent cellular cytotoxicity by therapeutic antibodies faces several limitations, especially for low affinity variant of the receptor.	The difficulty of development of mAbs lies in (1) the long and complex research and development process, involving knowledge and technologies from various fields and (2) extensive laws, regulations and industry standards in drug research and development, production, operation and use, and high requirements of standardized drug development for new entrants to the pharmaceutical industry.	Focus on major diseases, support in innovation, to achieve further breakthroughs. Enhancement of the key technologies to guarantee the safety, efficacy and quality control of mAbs. Continuous improvement of domestic production equipment, increasing automation, output amplification and higher requirements for plant facilities to support the rapid expansion of mAb production scale.
Bispecific Antibody (BsAb)	A BsAb is an artificial antibody that can simultaneously bind to two different types of antigens.	Potential effects on various cancers, the application to retarget effector cells of the immune system and stimulate them through the interaction to achieve an efficient lysis of tumor cells.	Low expression of the target structures. Non-human nature, limiting the dosage that can be given to patients. More challenges in chemical, manufacturing and control development.	The difficulty of development of BsAbs lies in (1) accurate assemble of heavy and heavy chains and heavy and light chains to reduce mismatch and (2) finding suitable pre-clinical evaluation models, which could be time-consuming and prolong the development process.	Application of BsAbs in cancer treatment in combination with T cell checkpoints blocking antibodies. Development of new structures of BsAbs with strong tumor cell killing activity and low levels of cytokine release. Increased engagement of mathematical modeling and simulation in the entire BsAb development process.
Antibody-drug Conjugate (ADC)	ADC consists of antibody, linker and cytotoxin. The antibody can specifically target a specific antigen which is expressed in the tumor cells; the linker acts as a bridge for antibody and cytotoxin. The linker is clearable or non-cleavable; the toxin small molecule should have high toxic activity and low immunity.	ADC drugs have larger tolerated doses, and smaller effective doses. ADCs are now also available in combination with other classes of drugs to enhance the effect of a single treatment. And ADC also targets non-oncology therapeutic areas.	The cytotoxin drug may be off-target in the blood, resulting in the killing of normal cells. ADC preparation cannot guarantee equal drug attachment for each antibody in each batch. Limited antigens are expressed only in tumor cells and not in normal cells.	The difficulty of development of ADC lies in (1) the design and development of a combination of antibody, linker and cytotoxin with optimized overall efficacy and safety, (2) the production of ADC and (3) application of advanced technologies, such as the biological coupling technology and the linker technology.	Modification of linkers to overcome issues in treating the multidrug resistance 1-expressing tumors. Integration of ADCs with other targeted agents and immune checkpoint inhibitors. Increased use of multiple, site-specific protein conjugation for the next generation of ADCs.
Multi-Specific Antibody (MsAb)	MsAb is an artificial antibody targeting two or more unique epitopes, which can bind more than one type of antigens.	MsAb constructs potentiate antibody-mediated effects, via simultaneously blocking multiple tumor-associated antigens, and/or triggering more intensified immune reactions. Multiple functions translate into improved response rates.	Hetero-dimerization of chains may make the molecule inefficient. Potential antigenic cytokine release syndrome. Tight white cell binding may change bio-distribution. Large molecules have less intertumoral penetration and they are hard to be cleared with risk of aggregation.	The difficulty of development of MsAbs lies in (1) their display of suboptimal physical and chemical properties, (2) challenges associated with thermal stability of MsAbs and (3) issues with proper and efficient assembly into large and complex molecular formats.	Therapeutic exploitation of intracellular neoantigens with MsAbs to overcome extracellular target scarcity. Improvement of expression and purification methods for simplifying the production of MsAbs with high yields and purity. Enhancement of computational methods for predicting antibody variants with favorable biophysical properties.

Source: Shabbir, A., Rasheed, A., Shehraz, H., Saleem, A., Zafar, B., Sajid, M., Ali, N., Dar, S. H., & Shehryar, T. (2021). Detection of glaucoma using retinal fundus images: A comprehensive review. Mathematical biosciences and engineering: MBE, 18(3), 2033 -2076. https://doi.org/10.3934/mbe.2021106; Labrijn, A. F., Janmaat, M. L., Reichert, J. M., & Parren, P. W. H. I. (2019). Bispecific antibodies: a mechanistic review of the pipeline. Nature reviews. Drug discovery, 18(8), 585 -608. https://doi.org/10.1038/s41573-019-0028-1; Gerber, D. E. (2008). Targeted therapies: a new generation of cancer treatments. American family physician, 77(3), 311-319.; Hollenbaugh, D., & Aruffo, A. (2002). Construction of immunoglobulin fusion proteins. Current protocols in immunology, 48(1), 10-19.; Bazarbachi, A. H., Al Hamed, R., Malard, F., Harousseau, J. L., & Mohty, M. (2019). Relapsed refractory multiple myeloma: a comprehensive overview. Leukemia, 33(10), 2343 -2357. https://doi.org/10.1038/s41375-019-0561-2; Ferrando-Díez, A., Felip, E., Pous, A., Bergamino Sirven, M., & Margelí, M. (2022). Targeted Therapeutic Options and Future Perspectives for HER2-Positive Breast Cancer. Cancers, 14(14), 3305. https://doi.org/10.3390/cancers14143305

Fusion protein antibodies is a bio-engineered protein that joins the biologically active protein domain with the fragment of an immunoglobulin. Bifunctional fusion proteins, constructed by fusing the genes of two proteins together, combine the functions of the parent proteins in order to improve their PK and PD properties, or to introduce novel approaches in drug delivery or targeting. By fusing one or more functional fragments of parent proteins, highly efficient targeted drugs can be formed. Fusion protein antibodies have prolonged metabolism time of the active protein domain *in vivo*. However, most fusion protein antibodies have poor stability and short half-life, which requires frequent dosing and is limited in clinical application. The difficulty of development of fusion protein antibodies lies primarily in the fierce competition with existing market players. For example, various fusion protein antibodies involving non-cytokine payloads have been developed for therapeutic applications; more than a dozen of Fc fusions have received FDA approval and many more Fc fusions are at various stages of therapeutic development. Efforts will be made to minimize the off-target activity of the antibody and the active protein domain and to overcome engineering and design challenges for all classes of fusion proteins. Development of novel fusion strategies and the incorporation of peptide and protein motifs in fusion protein development will further realize the potential of fusion protein antibodies.

The advantages and distinctive characteristics of fusion protein antibodies have translated into tremendous commercial success. Regeneron, Roche, and other pharmaceutical giants have generated significant sales from fusion protein antibody drugs.

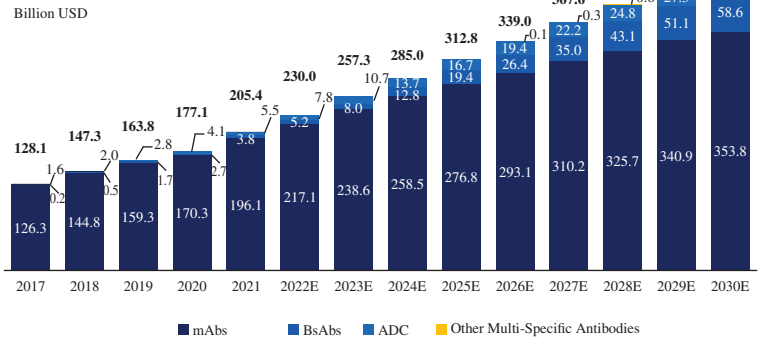
The following table sets forth a comparative analysis between BsAb and fusion protein antibodies:

Categories	Technical Challenges	Manufacturing Requirements	Molecular Stability	Clinical Efficacy
BsAb	The large molecular weight of BsAbs results in poor tumor permeability and a complex structure, which can lead to significant mismatch issues such as mismatch between heavy and light chains. Incorporating asymmetric structures can address these mismatch problems.	(1) High-throughput screening of potential therapeutic antibodies and the rapid generation of cell lines for recombinant human antibodies are necessary steps to achieve the production scale required for clinical testing. (2) The ability to genetically modify test animals to produce human antibodies is necessary. (3) Built-in purification technology is required to facilitate manufacturing at a commercial scale. (4) The production process for BsAbs is relatively mature, and the Fc region helps improve the antibody's solubility and stability, making production relatively convenient.	BsAb serum exhibits a long half-life, high molecular weight, and high stability, typically ranging from several days to tens of hours.	BsAbs are designed with two variable domains to elicit biological effects that require simultaneous binding to two targets. For instance, one variable domain can bind to tumor cells while the other variable domain can bind to cytotoxic immune cells. BsAbs are commonly utilized to treat solid tumors and solid tumors with different genetic mutations, including but not limited to lymphoma, hemophilia, leukemia, systemic lupus erythematosus, and neurodegenerative diseases such as Alzheimer's disease. The commercial clinical pipeline primarily focuses on cancer treatment and malignant tumors.
Fusion protein antibodies	Combining different components of the fusion protein that do not naturally occur together can result in instability with the composite molecule, posing manufacturing challenges such as aggregation during cell culture or purification steps. Furthermore, the fusion protein may have weak immunogenicity and require frequent administration.	The chemical manufacturing and control process for fusion proteins is more complex and less mature due to its differing structure compared to natural antibodies.	Fusion protein antibodies are primarily made up of flexible single-chain variable fragments and are considered smaller recombinant proteins that can be cleared by the kidneys. The typical serum half-life for fusion proteins is several hours which is shorter than that of BsAbs.	Fusion proteins are also frequently employed in the treatment of tumors, including solid tumors and hematological malignancies. However, the indications for fusion proteins are generally more limited, and their application range is not as broad as that of BsAbs.

In 2021, the global therapeutic antibody market grew to US$205.4 billion, representing a CAGR of 12.5% from 2017 to 2021, and is expected to reach US$312.8 billion in 2025 due to rising medical demand and innovative antibody pipelines, representing a CAGR of 11.1% from 2021 to 2025, and to further increase to US$443.1 billion in 2030, representing a CAGR of 7.2% from 2025 to 2030. The mAbs is the largest category in the global antibody market by revenue and accounted for over 95% of the market in 2021. While new biologics such as BsAbs, antibody-drug conjugates and other antibody types are still relatively new to the market, the anticipated market growth for these types of biologics is high given the breakthrough of technology and clinical studies.

Global Therapeutic Antibody Market Size, 2017-2030E

CAGR	mAbs	BsAbs	ADC	Other Multi-Specific Antibodies	Total
2017-2021	11.6%	114.8%	35.9%	-14.0%	12.5%
2021-2025E	9.0%	50.4%	31.7%	17.1%	11.1%
2025E-2030E	5.0%	24.8%	12.1%	120.0%	7.2%



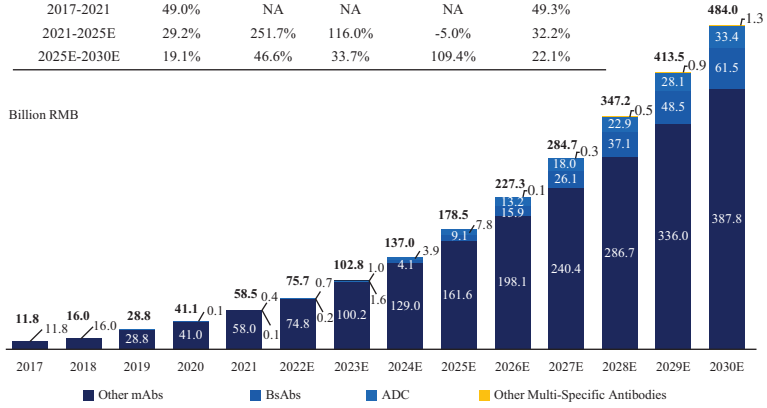
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, IARC, GLOBOCAN, Frost & Sullivan Analysis

Note: The market size for mAbs represents the market size of mAbs other than ADC.

China's therapeutic antibody market, in comparison, grew to RMB58.5 billion in 2021, representing a CAGR of 49.3% from 2017 to 2021, and is expected to rapidly grow and reach RMB178.5 billion in 2025 at a CAGR of 32.2% from 2021 to 2025, and RMB484.0 billion in 2030 at a CAGR of 22.1%.

Market Size of Therapeutic Antibody Market in China, 2017-2030E

CAGR	Other mAbs	BsAbs	ADC	Other Multi-Specific Antibodies	Total
2017-2021	49.0%	NA	NA	NA	49.3%
2021-2025E	29.2%	251.7%	116.0%	-5.0%	32.2%
2025E-2030E	19.1%	46.6%	33.7%	109.4%	22.1%



Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, NCCR, Frost & Sullivan Analysis

Growth Drivers and Future Trends of China Therapeutic Antibody Drug Market

The key growth drivers of China's therapeutic antibody drug market include: (a) the increasing patient pool due to the rising prevalence of chronic diseases brought by an aging population, accelerated urbanization and environmental changes; (b) the favorable regulatory policies issued by the Chinese government; (c) the Chinese government's emphasis on strengthening intellectual property protection; (d) the enlargement of the talent pool of research and development personnel that have extensive lab experience in the United States and Europe, thereby leveraging their experience to upgrade the research and development platforms of domestic companies; (e) the research and development collaboration with multinational corporations which facilitates the research and development capabilities of local players; and (f) the high market conversion rate of antibody drugs, as indications are gradually expanding to other disease areas.

The future trends of China's therapeutic antibody drug market mainly include: (a) the growing demands of China' antibody drugs market; (b) the progressive increase of favorable industrial policies in the antibody drugs market; (c) the high conversion rate of antibody drugs, which allows indications to expand into other disease areas; (d) the high return rate of antibody body drugs which leads to increased investment efforts from domestic pharmaceutical companies; (e) the development of new targets and therapies as a result of mAbs having a shorter history in China and the current extensive medical demands; (f) the increasing penetration of mAb drugs due to the expansion of the NRDL and the launching of biosimilars which will drive the growth of the entire pharmaceutical market; (g) the diversity of therapeutic antibody drugs as a result of rapid technological development; and (h) value creation through the continuous innovation of antibody technologies.

Global and China BsAb Market

Overview

A BsAb is an artificial protein that recognizes and specifically binds two antigens or epitopes. It simultaneously blocks the biological functions mediated by both antigens/epitopes or draws the cells of both antigens closer together. In recent years, a better understanding of the pathogenesis of various diseases and the rapid development of therapeutic mAbs have also contributed to the development and advancement of BsAbs. With the development of antibody construction, expression and purification techniques, dozens of structures have emerged from BsAbs. The applications and research of existing BsAbs are mainly focused on the field of oncology therapy, but also extend to other areas such as hemophilia and ophthalmology.

The development of BsAbs is a nascent field and faces many imminent risks and challenges. BsAbs are produced through cellular expression techniques, typically incurring higher production costs than the synthesis technologies used for small molecule drugs. In addition, BsAbs cannot be administered orally, thus the less convenient administration methods of BsAbs especially intravenous administration, increases treatment costs and safety risks associated with infusions.

Compared to monospecific antibodies, the design, research, and validation of the dual-specific binding mechanism of BsAbs, along with the molecular construction and preparation of BsAbs, are significantly more complex. This increases the difficulty and risk of developing BsAbs and the difficulty and cost of their production.

Compared to cell therapies, BsAbs cannot replenish functional cells in the body. Therefore, in situations where there is a deficiency of functional cells in the body, BsAbs may not be able to achieve optimal therapeutic effects.

The construction of bispecific molecules is more complicated than that of monospecific antibodies. From 2000 to the present, pharmaceutical companies worldwide have been continuously developing different bispecific molecule platform technologies, aiming for more stable and reliable platform structures. As a result, most drug molecules began entering clinical trials after 2015. Thus, the number of approved BsAb drugs is currently limited, and there are even fewer pipelines specifically for the treatment of MA and MPE. As of the Latest Practicable Date, there were only one BsAb (catumaxomab) applying for renewal of marketing authorization and one pipeline of BsAb (M701 of the Company) under clinical development globally that were specifically developed for the treatment of MA and MPE.

Currently, BsAbs are generally divided into two categories according to their structure: IgG-type structure and non-IgG-type structure. Between the two, the IgG-type structure can be further divided into two types: symmetric and asymmetric, where the asymmetric structure has obvious advantages. The diagram below illustrates the categories of BsAbs, including their advantages and disadvantages:

	Non-IgG	Symmetric IgG	Asymmetric IgG
Advantages	• Simple structure • The clinical dosage is low, less than one-tenth of the original amount of antibodies • Weak immunogenicity	• Similar to the structure and stability of natural IgG • Mature technology, high expression	• Solved the technical limitations of Knobs-into-Holes technology in common light chain • Realizes the bivalent binding of tumor antigens, which can reduce the toxicity caused by CD3 antibodies when binding to tumor antigens
Disadvantages	• Short half-life (only 2 hours) • Unstable structure, low expression and difficult process	• Limited spatial bispecific binding effect	• Long technical route, difficult design and process

Source: Frontiers in Immunology, 2021: 1555., Analysis and Characterization of Antibody-based Therapeutics. Elsevier, 2020: 167-179., Journal of Immunology Research, 2019, 2019., Antibodies, 2018, 7(3): 28., Journal of hematology & oncology, 2015, 8(1): 1-14., Frost & Sullivan Analysis

Comparison of BsAbs with Other Treatment Methods

Comparison with monoclonal therapies

BsAbs are structurally designed to target different antigen binding sites. For T cell-engaging BsAbs, one of their binding arms targets antigens and the other arm binds the labeled antigen on the effector T cell, which activates the effector T cells to kill tumor cells. The interaction with two different surface antigens induces the binding specificity and reduces side effects such as off-target toxicity. Further, since one disease modulator may play an essential role in several independent pathways and co-expression of different receptors has been found in many tumors, targeting two different growth-promoting receptors on a single tumor cell may increase the antiproliferative effect and help avoid the development of drug resistance. However, the safety and efficacy of BsAbs in treating cancer and its complications compared to their monoclonal antibody counterparts, which have been marketed or are currently going through clinical development in large amount, remain to be substantiated in clinical applications.

Comparison with combination therapies

The use of BsAbs compared to combination therapies with two monospecific drugs makes it possible to optimize expenses by reducing the cost of development and clinical trials. Additionally, BsAbs only require single administration compared to combination therapies that require multiple injections of two or more antibodies, simplifying the frequency and practice of administration. However, the safety and efficacy of BsAbs in treating cancer and its complications compared to combination therapies remain to be substantiated in clinical applications.

Comparison with current treatments for retinal disorders

Most treatments for retinal disorders target the vascular endothelial growth factor (VEGF), but not all patients respond to these treatments. BsAb drugs target two pathways simultaneously. Therefore, patients who are not sensitive to anti-VEGF therapies may benefit from blocking the other angiogenesis pathway. Studies have shown that more than 50% of patients were able to go 16 weeks or longer between treatments and more than 70% of patients were able to extend the treatment interval by 12 weeks or longer. However, the safety and efficacy of BsAbs in treating cancer and its complications compared to current treatments for retinal disorders remain to be substantiated in clinical applications.

Market Size

In 2021, the global BsAb market grew to US$3.8 billion, representing a CAGR of 114.8% from 2017 to 2021, and is expected to reach US$19.4 billion in 2025 due to breakthroughs of technology and clinical studies, representing a CAGR of 50.4%, and to further increase to US$58.6 billion in 2030, representing a CAGR of 24.8%. China's BsAb market size was RMB0.1 billion in 2021, but is expected to reach RMB9.1 billion in 2025, representing a CAGR of 251.7%, and to further increase to RMB61.5 billion in 2030, representing a CAGR of 46.6%. In terms of percentage of corresponding therapeutic antibody market, the market share of BsAb drugs globally and in China in 2022 are 2.3% and 0.3%, respectively.

The rapid growth of China's BsAb market size from 2021 to 2025 is mainly attributed to the following factors:

(i) Starting from a small base market: As of November 2020, China had only one marketed BsAb product, Emicizumab, which was launched in November 2018. Its indication, Hemophilia A, is a rare disease with a limited patient population and modest sales, resulting in a 2021 BsAb market size of only RMB0.1 billion. Thus, the rapid growth from 2021 to 2025 begins from a very small market base.

(ii) Rapid growth: Between December 2020 to June 2022, three BsAb products were launched in China: Blinatumomab in December 2020 and Cadonilimab in June 2022. These two products both generated substantial revenues within one to two years after their launch.

(iii) Significant growth potential: There are multiple products expected to enter the market in the near future. Furthermore, the pace of BsAb drug development and market promotion is expected to accelerate after the impact of the COVID-19 epidemic diminishes.

China's BsAb market is expected to grow at a CAGR of 196.0% from 2023 to 2025. According to Frost & Sullivan, the development trend of China's BsAb market from 2023 to 2025, having four BsAb products launched in 2023 and a rich pipeline under development, is comparable to that of China's anti-PD-1/PD-L1 mAb market from 2018 to 2020. China's anti-PD-1/PD-L1 mAb market grew at a CAGR of 278.3% from 2018 to 2020, with four PD-1/PD-L1 products launched in 2018.

Due to the limited number of marketed BsAb products globally and domestically, and the absence of any BsAb biosimilars, the growth rate of China's BsAb market is expected to remain high at a CAGR of 46.6% from 2025 to 2030.

Recently, other favorable policies in China such as the NMPA's "Opinions on Encouraging Pharmaceutical Innovation via Priority Review & Approval" (《關於鼓勵藥品創新實行優先審評審批的意見》) will also help streamline the drug approval process and accelerate drug launches in China.

Growth Drivers and Future Trends of China BsAb Market

The key growth drivers of China's BsAb drug market include: (a) the durability of the efficacy for BsAbs, as the synergistic effects of BsAbs reduce tumor cell escape and diminish the potential side-effects caused by mAbs, which subsequently improve therapeutic efficacy. Additionally, BsAbs can potentially increase binding specificity by interacting with two different cell-surface antigens instead of one, which also brings higher safety and efficacy; and (b) a potential for multiple applications, as the dual specificity of BsAbs opens up a wide range of applications, including redirecting T cells to tumor cells, blocking two different signaling pathways simultaneously, dual targeting of different disease mediators, and delivering payloads to targeted sites.

The future trends of China's BsAb drug market include: (a) the development of manufacturing technologies for BsAbs. The BsAb development has long been hampered by manufacturing related challenges, such as product instability, low expression yields and immunogenicity. Simplifying the structure and production procedures are keys to designing an ideal BsAb platform moving forward; (b) the continuous research and development efforts in evolving technologies that would enable BsAbs to treat solid tumors, where their treatment effects are currently limited; and (c) the expansion of indications for BsAbs, as BsAbs have the potential to go beyond the treatment of tumors and serve as an important modality for the treatment of other disease types such as inflammatory diseases; and (d) the proactive engagement of leading domestic pharmaceutical companies in the research and development of BsAbs drugs.

OVERVIEW OF MAJOR TARGETS OF THE COMPANY'S BISPECIFIC ANTIBODY DRUG CANDIDATES

The diagram below illustrates the comparative analysis of the targets of the Company's BsAb drug candidates:

Targets	Advantages	Limitations	Entry Barriers	Future Trends
EpCAM	EpCAM overexpresses on epithelial tumors, circulating tumor cells and cancer stem cells, and is associated with the proliferation, differentiation and adhesion of epithelial cancer cells. Because most solid tumors are of epithelial origin, EpCAM can be used as a tumor marker with potential application as effective diagnostic and therapeutic targets for multiple tumors.	The development of drugs targeting on EpCAM is difficult. EpCAM is not a very good target for mAb development, mainly because EpCAM is widely expressed on normal tissues which might cause safety issues, and mAb targeting EpCAM has limited efficacy. Lacking stratification of patients based on EpCAM makes it inefficient for clinical use.	The difficulty lies in the clinical development. There are technical barriers in the design of EpCAM targeted drugs with new mechanisms and better anti-tumor effect. More exploring studies are required in the selection of clinical indications and dosing regimens.	Developing therapies with new mechanisms, such as BsAbs, ADCs, and CAR-T cell therapies targeting EpCAM. Exploring local therapy in abdominal, thoracic, and urinary tracts. Studying EpCAM targeted drugs with companion diagnostics for cancers, establishing of precision medicine protocols, and researching the combination therapies of EpCAM targeted drugs and other drugs.
VEGF	VEGF plays important roles in angiogenesis of tumors and neovascular eye diseases, and anti-VEGF drugs have achieved great clinical benefits in oncology and ophthalmology. It is also an immunomodulator of the tumor microenvironment and promotes an immune suppressive microenvironment. VEGF targeted combination therapies with anti-PD-1 drugs have been approved for various indications such as lung cancer.	Although VEGF inhibitors showed prospective efficacy in clinical application, there are still barriers and challenges to surmount, such as to moderate clinical efficacy, mechanism-related toxicities and the occurrence of clinical resistance.	VEGF is currently one of the most popular targets and has a wide range of applications. The fierce market competition has put higher demands on the effectiveness and safety of new VEGF-based products.	Identifying novel combination strategies of VEGF inhibitors and multi-targets, especially dual-targets drug design is one of the hottest areas in tumor treatment to have synergistic antitumor effect and improved pharmacokinetic properties. Designing multi-targets drug and improving formulation for the clinical importance of VEGF for neovascular eye diseases.
HER2	HER2 overexpression is prevalent in many cancers, such as breast cancer, gastric cancer, bladder cancer, pancreatic cancer and ovarian cancer. HER2-high expression is found specifically in tumor tissue. Therefore, in the treatment of HER2-positive solid tumors, HER2 targeted therapies have better safety and efficacy than traditional chemotherapy.	The current HER2 targeted therapies have a poor effect on patients with HER2-low and -medium expression. Many patients with high HER2 over-expression still do not respond to HER2 targeted therapies, and may develop resistance to the therapies with the same mechanism after a period of treatment time.	HER2 is a well-studied therapeutic target. Currently, the competition for the developments of HER2 targeted mAbs and ADC drugs is very fierce. The entry barriers mainly include development of highly effective HER2 targeted drugs with new molecular structures, and selection of appropriate research methods for pre-clinical and clinical research.	Developing new types of HER2 targeted therapies. Exploring the combination of HER2 targeted drugs and other drug. Expanding indications of which HER2 targeted therapies can be used for treatment.
ANG2	ANG2 plays a key role in promoting angiogenesis and stability in vascular physiology. Activation of ANG/Tie2 signaling is important in the restoration of vascular integrity which is essential in the treatment of some eye disorders like DME and wAMD. In addition, ANG-2 levels are significantly elevated in the vitreous fluid of diabetic eyes, which makes it a new target of the anti-angiogenesis therapy.	The expression of ANG2 is complex, and is regulated by different mechanisms in different abnormal cells. Blocking of single ANG2 signaling is insufficient for druggability.	Because ANG1 and ANG2 are highly homologous, it is difficult to develop a targeted drug that is only specific to ANG2. For ophthalmic diseases, it is technically difficult to develop a high concentration formulations. How to improve the efficacy of ANG2 targeted drugs and to achieve industrialization are two key barriers to entry into this field.	Exploring the potential of combination therapies with other drugs to treat tumors clinically. Developing new regiments for the treatment of neovascular eye diseases.
CD38	CD38 plays vital roles in normal cell functions and tumor growth. CD38 is widely expressed on multiple hematological malignant cells with high expression level, which represents an ideal target for treatment of hematological malignant tumors, such as MM cells. Anti-CD38 mAbs kill tumor cells through ADCC, ADCP, CDC and inhibiton of enzyme activity. Besides, CD38 can regulate the immunosuppressive microenvironment via its enzyme activity, adhesion effects, and crosses with other signaling pathways, which shows its potential functions in solid tumor treatment.	The ORR and the MRD clearance rates of CD38 mAbs are low, and the treated MM patients are prone to relapse.	To improve the effectiveness of this target and the clearance of MRD, breakthroughs in some new technologies and new mechanisms of action are still needed.	Developing novel drugs targeting CD38, such as BsAbs. Exploring combination regimen of CD38. Expanding CD38 in areas other than MM treatment. Strengthening the CD38 treatment for solid tumors, companion diagnostics and MRD detection.
PD-1/PD-L1	PD-1/PD-L1 targeted therapies possess broad-spectrum anti-tumor effects. Patients with effective response to PD-1/PD-L1 can achieve long-term survival with lower side effects. The treatment is readily available and inexpensive.	PD-1/PD-L1 targeted therapies are ineffective for some types of cancers. Among the effective cancers, majority of patients have no response to the PD-1/PD-L1 immunotherapy or have gained resistant.	It is difficult to improve the effectiveness of existing antibodies with a single PD-1/PD-L1 target.	Improving clinical responses based on a comprehensive understanding of the resistance mechanisms of PD-1/PD-L1 inhibitors and how to overcome them. Studying the PD-1/PD-L1 targeted BsAbs and the combination therapies of PD-1/PD-L1 blockade with adjunctive strategies.
TGF-β	TGF-β has the functions of regulating cell growth, differentiation, ECM remodeling, promoting angiogenesis, endothelial mesenchymal transition, and regulating immunity. Abnormalities of TGF-β are associated with inflammation, fibrosis, tumors, and other diseases, making it an attractive target for disease treatment.	The mechanism of the pathway is complex; TGF-β plays different roles in different stages of tumor development. Monotherapies with a single TGF-β targeted drug is still difficult to reach a desired efficacy.	Screening for drug molecules with good safety profiles and a good inhibitory effect on TGF-β pathway and obtaining ways to inhibit TGF-β to improve the therapeutic effect are two barriers to the development of this target.	Developing BsAbs with TGF-β inhibitory function and combination therapies with other drugs. Developing TGF-β-related biomarkers associated with efficacy, including cytokines, cancer stages and pathological characteristics of the tumors (degree of fibrosis, characterization of the immune microenvironment, etc.).
CD3	CD3 is the initial signal for T-cell activation and has well-defined functions. CD3 targeted mAbs result in T-cell clearance, which has practical applications in type 1 diabetes and organ transplantation. Antibodies that can target both tumor antigens and CD3 can directly activate T cells and perform immune killing function on target cells, bypassing MHC and other pathways. CD3 targeted BsAbs account for the majority of current marketed BsAbs. Compared with cell-based drug, the production of CD3 targeted therapies can be scaled up more easily, treatment costs are lower, and safety is higher.	Pre-clinical models for pharmacological efficacy evaluation with high correlation to clinical translation are difficult to establish. The activation of CD3 may increase CRS risk. The starting dose is usually low when entering the clinical trials, requiring more time for dose escalation and administration method exploration.	It is difficult to have the self-developed genetic engineering technologies of humanized activated CD3 antibodies and CD3 BsAbs. The manufacture of BsAbs, establishment and assessment of pre-clinical models and the technical complexity of clinical studies, are all barriers of this field.	Reducing the safety risk through molecular structure and affinity adjustment. Continuously expanding the application of CD3 targeted therapies in solid tumors. Conducting research on combination therapies.

Source: Relevant research papers, such as Macdonald, J., Henri, J., Roy, K., Hays, E., Bauer, M., Veedu, R. N., Pouliot, N., & Shigdar, S. (2018). EpCAM Immunotherapy versus Specific Targeted Delivery of Drugs. Cancers, 10(1), 19. https://doi.org/10.3390/cancers10010019; Zhao, Y., Guo, S., Deng, J., Shen, J., Du, F., Wu, X., Chen, Y., Li, M., Chen, M., Li, X., Li, W., Gu, L., Sun, Y., Wen, Q., Li, J., & Xiao, Z. (2022). VEGF/VEGFR-Targeted Therapy and Immunotherapy in Non-small Cell Lung Cancer: Targeting the Tumor Microenvironment. International journal of biological sciences, 18(9), 3845–3858. https://doi.org/10.7150/ijbs.70958

Note: Local therapy refers to the topical use of drug to treat lesions.

CD3 TARGETED BISPECIFIC ANTIBODY MARKET

CD3 Targeted BsAbs

T cell-based therapies can be mainly divided into two classes depending on the different mechanisms of actions: one class against immunosuppressive factors represented by immune checkpoint inhibitors, and the other class focusing on immunostimulatory pathways represented by CAR-T cells and T cell-engaging BsAbs. CAR-T cell therapy is an adoptive cell therapy that genetically engineers T cells to express a CAR comprising intracellular T cell signaling domains and an extracellular antigen-recognition structure targeting tumor-associated antigens (TAA), redirecting and activating T cells to eradicate malignant cells. The alternative approach to redirecting T cells against target cells is T cell-engaging BsAbs which do not require genetical engineering, and bind TAAs on cancer cells and targets on T cells with their two arms, thereby engaging effective T cells and tumor cells.

CD3 is a protein complex and T cell co-receptor that is involved in activating both the cytotoxic T cell and T helper cells. These chains are associated with the T cell antigen recognition receptor (TCR) and the CD3-zeta which is a homodimer to generate an activation signal in T lymphocytes. Due to the invariant property of CD3 chains in the TCR, CD3 is always selected as cell surface target. The CD3 BsAbs can employ different types of T cells and are not limited to tumor-specific T cells, contrary to the key requirement for effective immune checkpoint therapy. CD3-targeting and T cell-engaging BsAbs require complete suppression of fragment crystallizable-mediated effector functions in order to minimize off-target toxicity and to maximize therapeutic efficacy. In recent years, CD3 has been an emerging target in BsAbs development for cancer treatment. Around 45% of globally marketed BsAbs and BsAbs in clinical development target CD3.

As of the Latest Practicable Date, with respect to the indications covered by the Company's existing pipeline for cancer treatment, there was one CD3 targeted antibody drug approved for the treatment of multiple myeloma (MM) and one for the treatment of uveal melanoma globally. No other marketed CD3 targeted antibody drug has been approved for the treatment of MM, solid tumors, MA and MPE. The following table sets forth the details of the two aforementioned marketed CD3 targeted antibody drugs globally as of the Latest Practicable Date:

Global Marketed Drugs

Product	Drug Name	Developer	Target	Drug Type	Indication	Approval Date	Price (USD)
TECVAYLI	Teclistamab	Janssen Biotech, Inc.	BCMA, CD3	BsAb	MM	October 25, 2022	10mg/ml 3ml: 1,873
KIMMTRAK	Tebentafusp	Immunocore Ltd.	GP100, CD3	ADC	Uveal Melanoma	January 25, 2022	100mcg/0.5ml 0.5ml: 20,257

Source: FDA, NKEXnews, Annual Reports of Listed Medical Companies, Clinical Trials, Frost & Sullivan

As of the Latest Practicable Date, there were 75 and 21 CD3 targeted antibody drug candidates or fusion proteins for the treatment of MA, MPE, MM and solid tumors under clinical development globally (excluding China) and in China, respectively, according to the CDE and the ClinicalTrials.gov websites.

Scientific Barriers to CD3 Targeted BsAbs

The development of CD3 targeted BsAb drugs currently faces challenges including: (a) the risk of on-target off-tumor toxicities on solid tumors, since solid tumor-associated antigens are often also expressed on tissues of healthy organs, which can lead to immune pathology and organ failure with potential fatality; (b) the complex structural characteristics of the CD3 protein which leads to difficulties in designing effective compounds with specific binding according to their structure; and (c) the presence of multiple immunosuppressive cell types in the tumor microenvironment of solid tumors, which compromises the quality of effector T cells, and reduces the effectiveness of the immunological synapse created by the CD3 targeted BsAbs.

Future Trends of CD3 Targeted BsAbs

The future trends of CD3 targeted BsAbs mainly include: (a) the potential combination of CD3 BsAbs with other therapies to reach better treatment outcomes; (b) the increased focus on solid tumors, as several CD3 BsAbs have been successfully used in the clinic for the treatment of hematologic tumors, the indications are actively expanding towards solid tumors; and (c) the proactive development of new strategies to mitigate the toxic side effects of CD3 BsAb treatments.

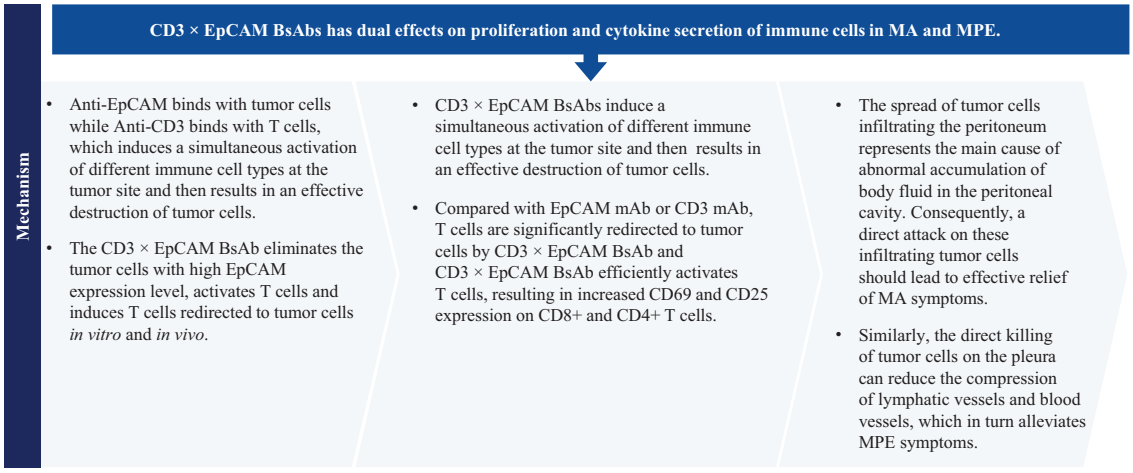
EpCAM × CD3 Targeted BsAb

Mechanisms of EpCAM × CD3 Targeted BsAbs

EpCAM is an attractive target for antibody therapy of oncology. EpCAM is one of the most frequently and most intensely expressed tumor-associated antigens and can be observed in over 90% of common types of cancers causing malignant ascites and malignant pleural effusion.

The development of anti-EpCAM and anti-CD3 BsAbs provide an emerging alternative to address the scientific barriers to CD3 targeted BsAbs.

The diagram below illustrates the mechanism of action of EpCAM × CD3 targeted BsAb in malignant ascites (MA) and malignant pleural effusion (MPE) treatments:



Source: Medicina, 2019, 55(8): 490., Cellular and Molecular Life Sciences, 2018, 75(3): 509-525., Cancer treatment reviews, 2010, 36(6): 458-467., International journal of cancer, 2014, 135(11): 2623-2632., Blood, The Journal of the American Society of Hematology, 2001, 98(8): 2526-2534., Frost & Sullivan Analysis

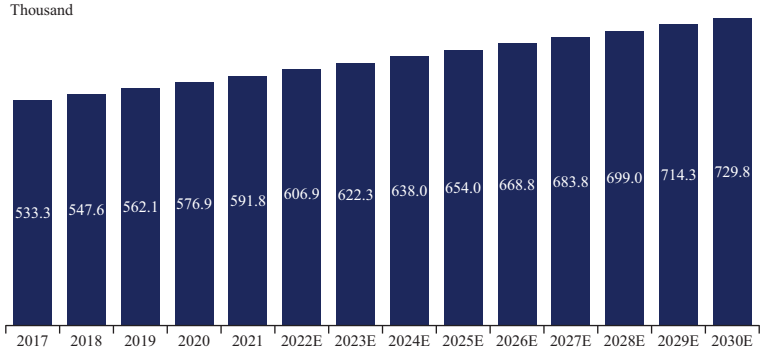
Malignant Ascites (MA) and Malignant Pleural Effusion (MPE)

MA is the accumulation of fluid in the peritoneal cavity resulting from the growth of primary or metastatic malignant neoplasms in the peritoneum. MA may be associated with a variety of neoplasms, including ovarian, breast, gastric, lung, and pancreatic cancers. MPE is the collection of fluid in the pleural cavity resulting from malignant disease. Malignant pleural effusions often contain free floating malignant cells. This can cause the patient to feel short of breath and/or experience chest discomfort. MPE is a fairly common complication in different cancers. The most common etiologies for MPE are lung cancer, breast cancer, lymphoma, ovarian cancer and gastric cancer. MPE is observed on approximately 45% lung cancer patients, 2% to 11% breast cancer patients, 41.6% lymphoblastic lymphoma patients, and 33% ovarian cancer patients.

The incidence of MA in China has grown from 533.3 thousand in 2017 to 591.8 thousand in 2021, representing a CAGR of 2.6%. It is expected that the prevalence will increase to 654.0 thousand in 2025, and 729.8 thousand in 2030, at a CAGR of 2.5% and 2.2%, from 2021 to 2025 and from 2025 to 2030, respectively.

China Incidence of MA, 2017-2030E

Period	CAGR
2017-2021	2.6%
2021-2025E	2.5%
2025E-2030E	2.2%



Source: NCCR, Practical Pharmacy and Clinical Remedies. 2020,23(10):905-908., Chinese Journal of Gastroenterology and Hepatology. 2017, Hepatology International. 2013 Mar;7(1):188-198., 26(04):476-478., Frost & Sullivan Analysis

According to Frost & Sullivan, the addressable MA patients of M701 in China in 2030 is estimated to be 540.7 thousand. The table below sets forth the basis and assumption of the estimation of Frost & Sullivan.

Addressable MA Patients of M701 in China	Unit	2030E
Incidence of MA[(1)]	Thousand	729.8
Treatment Rate[(2)]	%	82.3
Local Therapy Rate[(3)]	%	90.0
Addressable Patients[(4)]	**Thousand**	**540.7**

Notes:

(1) The source of MA incidences in China is Globocan.

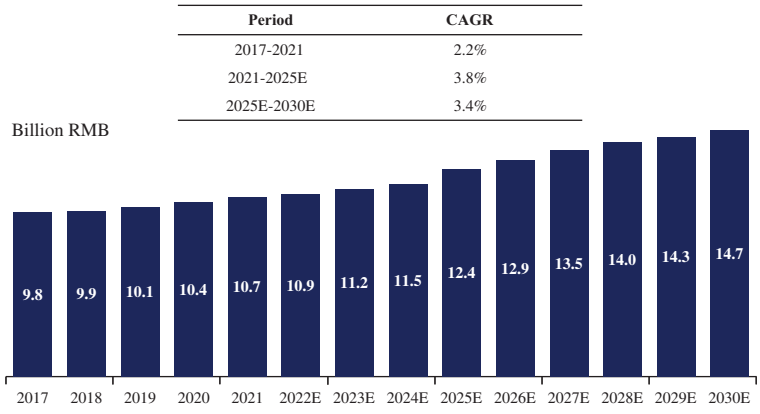
(2) Treatment Rate means the percentage of MA patients who are willing to receive any treatment for MA.

(3) Local Therapy Rate means, out of all the MA patients who are willing to receive any treatment for MA, the percentage of such patients who need to receive local therapy for MA (as versus to systematic treatment for tumor control).

(4) MA patients who are willing to receive any treatment for MA and is in need of a local therapy are addressable patients for M701 (i.e., by assuming that all the MA patients that are willing to receive any treatment for MA and is in need of a local therapy may choose to use M701). In this table, the number of addressable patients (540.7 thousand) is arrived by multiply the Incidence of MA by the Treatment Rate and Local Therapy Rate (729.8 thousand * 82.3% * 90.0%).

The market size of MA therapies grew from RMB9.8 billion in 2017 to RMB10.7 billion in 2021, representing a CAGR of 2.2%. It is predicted that the number will continue to grow, and reach RMB12.4 billion by the year of 2025, and RMB14.7 billion by the year of 2030, with CAGR of 3.8% and 3.4%, respectively. Taking into consideration the relatively small patient group size for MA, the market size for MA treatment is relatively significant because approximately 50%-60% of MA patients opt for the expensive anti-angiogenesis drugs to manage MA, despite that many current medical treatment methods for MA, primarily paracentesis, diuretics such as spironolactone, hyperthermic intraperitoneal chemotherapy and manual aspiration, are less costly in nature.

China Market Size of MA Therapies, 2017-2030E



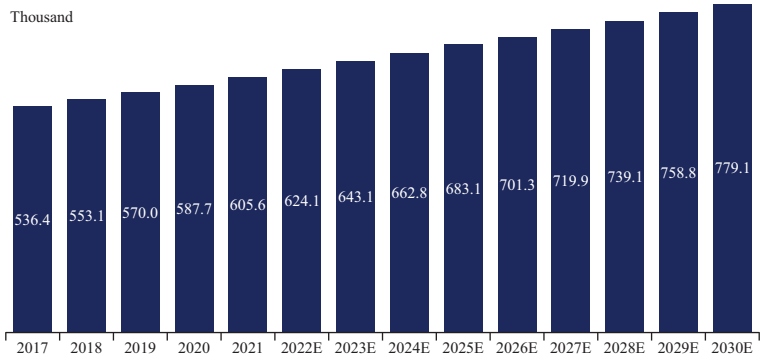
Source: Annual Reports of Listed Medical Companies, NCCR, MOHRSS, Practical Pharmacy and Clinical Remedies. 2020,23(10):905-908., Chinese Journal of Gastroenterology and Hepatology. 2017, Hepatology International. 2013 Mar;7(1):188-198., 26(04):476-478., Frost & Sullivan Analysis

Comparing with the rapid growth of the oncology drug market in China (which is projected to reach RMB400.5 billion in 2025 and RMB651.3 billion in 2030, representing a CAGR of 14.7% from 2021 to 2025 and 10.2% from 2025 to 2030), the overall growth rate for the China market size of MA therapies is comparatively stable, mainly as (a) the continually emerging expensive innovative treatment pipelines in the China oncology drug market, whereas (b) the relatively slower pace in the launch of expensive, innovative MA therapies in China market.

The incidence of MPE in China has grown from 536.4 thousand in 2017 to 605.6 thousand in 2021, representing a CAGR of 3.1%. It is expected that the prevalence will increase to 683.1 thousand in 2025, and 779.1 thousand in 2030, at a CAGR of 3.1% and 2.7%, from 2021 to 2025 and from 2025 to 2030, respectively.

China Incidence of MPE, 2017-2030E

Period	CAGR
2017-2021	3.1%
2021-2025E	3.1%
2025E-2030E	2.7%



Source: NCCR, Medicine, 2020, 99(39)., Journal of ethnopharmacology, 2020, 249: 112412, Journal of Practical Oncology 2021, 36(01): 89-94, Frost & Sullivan Analysis

According to Frost & Sullivan, the addressable MPE patients of M701 in China in 2030 is estimated to be 552.1 thousand. The table below sets forth the basis and assumption of the estimation of Frost & Sullivan.

Addressable MPE Patients of M701 in China	Unit	2030E
Incidence of MPE[(1)]	Thousand	779.1
Treatment Rate[(2)]	%	78.7
Local Therapy Rate[(3)]	%	90.0
Addressable Patients[(4)]	**Thousand**	**552.1**

Notes:

(1) The source of MPE incidences in China is Globocan.

(2) Treatment Rate means the percentage of MPE patients who are willing to receive any treatment for MPE.

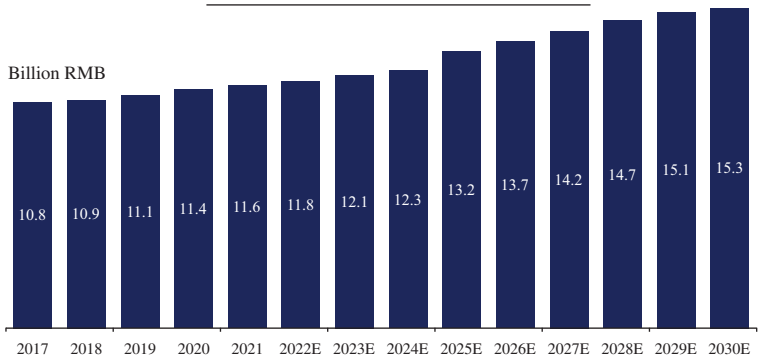
(3) Local Therapy Rate means, out of all the MPE patients who are willing to receive any treatment for MPE, the percentage of such patients who need to receive local therapy for MPE (as versus to systematic treatment for tumor control).

(4) MPE patients who are willing to receive any treatment for MPE and is in need of a local therapy are addressable patients for M701 (i.e., by assuming that all the MPE patients that are willing to receive any treatment for MPE and is in need of a local therapy may choose to use M701). In this table, the number of addressable patients (552.1 thousand) is arrived by multiply the Incidence of MPE by the Treatment Rate and Local Therapy Rate (779.1 thousand * 78.7% * 90.0%).

The market size of MPE therapies grew from RMB10.8 billion in 2017 to RMB11.6 billion in 2021, representing a CAGR of 1.8%. It is predicted that the number will continue to grow, and reach RMB13.2 billion by the year of 2025, and RMB15.3 billion by the year of 2030, with CAGR of 3.3% and 3.0% respectively. Taking into consideration the relatively small patient group size for MPE, the market size for MPE treatment is relatively significant because approximately 50%-60% of MPE patients opt for the expensive anti-angiogenesis drugs to manage MPE, despite that many current medical treatment methods for MPE, primarily paracentesis, diuretics such as spironolactone, hyperthermic intraperitoneal chemotherapy and manual aspiration, are less costly in nature.

China Market Size of MPE Therapies, 2017-2030E

Period	CAGR
2017-2021	1.8%
2021-2025E	3.3%
2025E-2030E	3.0%



Source: Annual Reports of Listed Medical Companies, NCCR, MOHRSS, Medicine, 2020, 99(39)., Journal of ethnopharmacology, 2020, 249: 112412, Journal of Practical Oncology 2021, 36(01): 89-94, Frost & Sullivan Analysis

Comparing with the rapid growth of the oncology drug market in China (which is projected to reach RMB400.5 billion in 2025 and RMB651.3 billion in 2030, representing a CAGR of 14.7% from 2021 to 2025 and 10.2% from 2025 to 2030), the overall growth rate for the China market size of MPE therapies is comparatively stable, mainly as (a) the continually emerging expensive innovative treatment pipelines in the China oncology drug market, whereas (b) the relatively slower pace in the launch of expensive, innovative MPE therapies in China market.

Competitive Landscape of MA and MPE Treatments

The currently available MA and MPE treatments mainly focus on curing primary tumors in early-stage patients or relieving symptoms in advanced cancer patients. However, MA and MPE are frequently associated with malignancies in several organs that have poor prognosis; therefore, advanced cancer patients rarely benefit from marketed drugs. To address this issue, innovative drugs specific to MA and MPE are currently under development.

The favorable results of the Phase I/II study on catumaxomab for MPE treatment demonstrated the efficacy of EpCAM × CD3 targeted BsAbs in MPE treatment. The Phase I clinical trial of catumaxomab in treating solid tumors has indicated that the intravesical therapy with catumaxomab is well tolerated and shows encouraging preliminary efficacy in patients with high-risk non-muscle-invasive bladder cancer.

According to public information, as of the Latest Practicable Date, there were one drug applying for renewal of marketing authorization and six pipelines of innovative therapies under clinical development globally that were specifically developed for the treatment of MA and MPE, including two BsAbs, three cell therapy pipelines and one polypeptide pipeline and one pipeline of other proteins, as illustrated below.

Global Pipeline

Product	Developer	Highest Clinical Stage	Indication	Region	Drug Type	Target	First Posted Date[(1)]
Catumaxomab	TRION Pharma GmbH and Neovii Biotech GmbH	Approved in 2009, withdrew from market in 2017, applied for renewal of the marketing authorization in 2022	Cancer, Neoplasms, Carcinoma, MA	France, Germany, Italy, Spain	BsAb	EpCAM, CD3	–
ENDOSTAR™	Jiangsu Simcere Pharmaceutical Co., Ltd.	Phase III	MPE, Malignant Peritoneal Effusion	China	Other Protein	Endostatin	2021/05/27
M701	the Company	Phase II	MA	China	BsAb	EpCAM, CD3	2021/07/23
M701	the Company	Phase Ib/II	MPE	China	BsAb	EpCAM, CD3	2022/08/08
GAIA-102	Gaia BioMedicine Inc; Kyushu University Hospital	Phase II	MA, Stomach Neoplasms, Pancreatic Neoplasms, Carcinoma, NSCLC	Japan	Cell Therapy	–	2021/11/19
RSO-021	RS Oncology LLC	Phase I/II	MPE, Malignant Pleural Mesothelioma, Mesothelioma, Solid Tumor	United Kingdom	Polypeptide	–	2022/02/07
VAK	Wuhan Binhui Biotechnology Co., Ltd.	Phase I	MPE, Malignant Peritoneal Effusion	China	Cell Therapy	–	2022/09/29
IFN-γ and CIK cells, Tcm cells or CAR-T cells	Affiliated Hospital of Jiangnan University	Phase I	MPE	China	Cell Therapy	–	2022/03/07

Source: NMPA, CDE, FDA, ClinicalTrials.gov, Frost & Sullivan Analysis

(1) "First Posted Date" in terms of global clinical trials refers to the date when the study corresponding to the global highest clinical phase (except China) was first available on ClinicalTrials.gov after the National Library of Medicine has concluded its quality control review; "First Posted Date" in the context of China clinical trials refers to the date when the study corresponding to the highest clinical phase in China was first available on chinadrugtrials.org.cn after the Center for Drug Evaluation (CDE) has concluded its review. The CDE is an affiliated institution of the NMPA.

Among them, catumaxomab (developed by TRION Pharma GmbH and Neovii Biotech GmbH) is the world's first marketed BsAb and has two targets identical to M701 which was approved in 2009 for the treatment of MA. Upon the initial commercial launch of catumaxomab in 2009, based on public information, the medical community's understanding of immunotherapy and BsAb was not fully developed, which limited the comprehension of the mechanism of actions of catumaxomab, resulting in a relatively cautious approach towards the clinical application of the drug. Moreover, based on public information, the developers of catumaxomab fell short in formulating a market-oriented marketing strategy for catumaxomab, which led to poor sales performance after its launch and its subsequent withdrawal from the market in 2017. Catumaxomab was marketed in Europe only and the withdrawal of catumaxomab only impacted the Europe market. The withdrawal of catumaxomab was primarily due to timing and sales strategy instead of safety and efficacy concerns. Despite of that, as the world's first BsAb drug, the withdrawal of catumaxomab did impact the overall perception of BsAbs within the medical community for a period of time. However, this perception has gradually improved with the increase in marketed BsAb drugs and their clinical use. Catumaxomab demonstrated manageable safety and encouraging efficacy during its clinical use. Therefore, the developers of catumaxomab applied for the renewal of the EMA marketing authorization of the drug for the treatment of MA in August 2022, which is currently under review.

In addition, LintonPharm Co., Ltd., a Guangzhou-based clinical-stage biopharmaceutical company, is evaluating catumaxomab in a Phase III clinical trial for stomach neoplasms, advanced gastric carcinoma with peritoneal metastasis, and a Phase I/II clinical trial for non-muscle-invasive bladder cancer in China. Based on publicly available information, LintonPharm are developing catumaxomab in collaboration with LINDIS Biotech, a research partner of TRION Pharma GmbH. LINDIS Biotech is also evaluating catumaxomab in a Phase I clinical trial for urinary bladder neoplasms in German. Catumaxomab was marketed in Europe only and the withdrawal of catumaxomab only impacted the Europe market.

As advised by Frost & Sullivan and according to public information, the following table sets forth BsAb pipelines targeting EpCAM and CD3 and mAb, antibody fusion protein and CAR-T pipelines targeting EpCAM currently under clinical development globally. As of the Latest Practicable Date, these competitors have not developed their EpCAM × CD3 drug candidates for the treatment of MA/MPE, however there is no guarantee that they will not expand into the MA/MPE treatment market with these drug candidates in the future.

Product	Developer	Drug Type	Target	Highest Clinical Phase	Region	First Posted Date	Indication
BA3182	BioAtla	BsAb	EpCAM, CD3	I	United States	4/1/2023	Advanced Adenocarcinoma
M701	Our Company	BsAb	EpCAM, CD3	I/II	China Mainland	9/30/2022	MA, MPE, Solid Tumor
Catumaxomab	LintonPharm Co., Ltd.	BsAb	EpCAM, CD3	III	China Mainland	10/6/2020	Stomach Neoplasms Advanced Gastric Carcinoma With Peritoneal Metastasis, Non-Muscle-Invasive Bladder Cancer
Catumaxomab	LINDIS Biotech	BsAb	EpCAM, CD3	I	German	7/7/2020	Urinary Bladder Neoplasms
AM-928	AcadeMab Biomedical	mAb	EpCAM	I	United States	1/7/2023	Solid Tumors
VB4-845	Qilu Pharmaceutical Co., Ltd.	Antibody fusion protein	EpCAM	III	China Mainland	4/13/2021	Non-Muscle Invasive Bladder Cancer
TM4SF1- positive chimeric antigen receptor T-cell therapy, EpCAM- positive chimeric antigen receptor T-cell therapy	Shanghai Biomedunion Biotechnology Co., Ltd.	CAR-T	EpCAM, TM4SF1	NA	China Mainland	10/29/2019	Solid Tumors

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

In addition to the above pipelines, Amgen Inc. commenced a multicenter Phase I clinical trial of solitomab, a bispecific EpCAM×CD3 T-cell engager BsAb in patients with refractory solid tumors in 2008. According to public information, Amgen Inc. has removed solitomab from its pipeline update since 2015, indicating that it may have suspended the clinical development plan for the drug candidate. We have not learned from public information that solitomab has safety or effectiveness issues. Amgen's suspension of this pipeline may be due to strategic considerations.

In terms of MA and MPE treatment, other proteins refer to protein drugs other than mAbs, BsAbs, MsAbs, or antibody fusion proteins, which include cytokines, growth factors, or truncated forms of factors such as IL-2 and endostatin. In short, other proteins do not contain any fragments of antibodies as they are commonly broad-spectrum inhibitors without particular targets. As a result, when compared with BsAbs that have specific targets, other proteins display lower selectivity and lower efficacy.

Treatment Paradigm for MA and MPE in China

The following table sets forth the treatment paradigm for MA and MPE in China and globally. Given that MA and MPE are complications of cancer and the limited numbers of drug candidates approved for MA and MPE, the current treatment paradigm for MA and MPE do not distinguish between first-line/second-line/later-line therapies.

Treatment Paradigm of MPE[1]		
Thoracentesis	**Pleurodesis**	**Indwelling Pleural Catheter (IPC)**
• Thoracentesis is an aprocedure where oncologists or thoracic surgeon may use to draw the fluid or air out from the pleural cavity, which could relieve the dyspnoea or other complications.	• Pleurodesis is a procedure in which a chemical is administered into the chest cavity after the pleural fluid has been drained to promote adhesion between the lung and chest wall, there by reducing the risk of new fluid build-up. This procedure can be performed either by placing a small catheter between the ribs into the fluid and administering the chemical through the tube or by using thoracoscopy to spray the chemical onto the inside of the chest wall within the pleural space.	• An indwelling pleural catheter is a small catheter that is inserted under the skin and into the pleural fluid, which enables repeated drainage at home to alleviate symptoms. These catheters are implanted as an outpatient procedure using local anesthesia. The catheter may help the lung eventually fully expand up to the chest wall. In many patients, once the fluid build-up is resolved, the catheter can be removed after 2-3 months.
Treatment Paradigm of MA		
Conventional Management	**Hyperthermic Intraperitoneal Chemotherapy**	**Newer modalities**
• Therapeutic paracentesis is a useful option for achieving rapid symptom relief. Large volume paracentesis, up to 5 liters, can be performed without significant complications. • Peritoneovenous shunts are recommended when the patient's life expectancy is more than 3 months.	• The rationale behind hyperthermic intraperitoneal chemotherapy includes cytoreduction by prolonged contact with tumor nodules, selective cytotoxicity due to protein denaturation, impaired DNA repair due to hyperthermia, and hyperthermia-induced vasodilation, which improves tumor oxygenation.	• Treatment of antibodies against cellular adhesion molecules (e.g., EpCAM) such as Catumaxomab after therapeutic paracentesis have been linked to prolonged paracentesis-free survival, enhanced quality of life, and extended overall survival.

Intended position and clinical focus of the Company's drug candidate

Source: CMA, Biospace, The Oncology Nurse

Note:

(1) According to Frost & Sullivan, M701 represents an innovative treatment for MPE and has not yet been included in the treatment paradigm of relevant clinical guidelines.

The following table sets forth the features and limitations of different treatment therapies.

The following table sets forth features and limitations of treatments for MA and MPE patients.

Treatment		Features	Limitations
Surgical Procedures(1)		Therapeutic paracentesis and indwelling drainage catheter could directly remove the effusions and relieve the symptoms, such as chest/abdominal pain, difficulty breathing and intestinal obstruction. Most widely accepted palliative treatments in several guidelines for MA/MPE management.	Surgical treatments cannot stop relapse of effusions accumulation and symptoms, which requires repeated surgical paracentesis, and lead to several complications, including hypoalbuminemia, pneumothorax, bleeding and intestinal obstruction. Those complications will lead to increased morbidity, mortality, and healthcare cost.
Local Therapy	Chemotherapy	Medicines are directly injected into cavities, which helps to reach the ideal concentrations and enhances their toxicity to tumor cells.	Chemotherapy is not an approved or recommended option for MPE/MA treatment due to limited efficacy, high relapse rate and insufficient clinical evidence. Repeated local chemotherapy may cause the peritoneal adhesion which will prevent further treatments. Also, the chemotherapy always causes side effects such as hematopoietic cytotoxicity, fatigue, nausea and hair loss etc.
	Pleural sclerosis	Pleurodesis makes inflammatory reaction between visceral pleura and parietal pleura, and fibrous adhesion occurs, so as to achieve the purpose of eliminating effusion.	Pleurodesis cannot be applied for MA in China due to lack of medical talc powder and it is only suitable for MPE treatment. Due to its relatively large side effects, it is only suitable for patients with good physical conditions.
	Immunosuppressants	Immunosuppressants can seal the serosal cavity by producing chemical inflammation, and also induce a variety of immune factors to strengthen the immune functions of the body to kill tumor cells	Immunosuppressants are not an approved and recommended option for MPE/MA treatments due to limited efficacy, high relapse rate and insufficient clinical evidence.
	Anti angiogenic drugs	Anti-angiogenic drugs can down-regulate the signaling pathways (e.g. VEGF) on the surface of tumor cells related to angiogenesis and changes in vascular permeability, thereby inhibiting tumor growth and differentiation, anti-tumor, and reducing effusion.	Anti-angiogenic drugs are not approved and recommended for MPE/MA treatment due to limited efficacy, high relapse rate, and insufficient clinical evidence. The anti-angiogenic drugs usually required combination treatments to achieve better effects.
	New modalities	Antibodies against cellular adhesions molecules like EpCAM such as Catumaxomab after therapeutic paracentesis are associated with prolonged paracentesis-free survival, improved quality of life and prolonged overall survival	Currently, there are no clinical trials that can prove its efficacy.

Intended position and clinical focus of the Company's drug candidate

Source: CSCO, NCCN

Abbreviation: Local therapy refers to the topical use of drug to treat lesions.

Note:

(1) Surgical procedures includes thoracentesis, pleurodesis, and indwelling pleural catheter for the treatment of MPE and therapeutic paracentesis (one of conventional management procedure) for the treatment of MA.

Currently, chemotherapy, immunosuppressants, and anti-angiogenic drugs have not been approved by the NMPA for the treatment of MA or MPE or included in the recommendations of clinical guidelines for MA or MPE in China. These therapies are listed in the table of features and limitations of treatments for MA and MPE above because they are incorporated into certain expert consensus for the treatment of MA and MPE in China. Expert consensus is usually based on weak evidence from one or two non-registration clinical studies, which makes it less influential in guiding clinical practice. In contrast, clinical guidelines are generally based on the results of large-scale randomized controlled Phase III trials and are widely recognized by clinicians.

Future Trends and Needs of MA and MPE Treatment

The future trends of the treatment of MA and MPE treatment mainly include: (a) the development of biomarkers as diagnostic and monitoring tools for MA and MPE, which is part of the current movement towards personalized medicine; (b) the continuous research and innovation of prominent pharmaceutical companies which will contribute to a more effective and cost-effective treatment; and (c) treatments gravitating towards patient outcomes and quality of life.

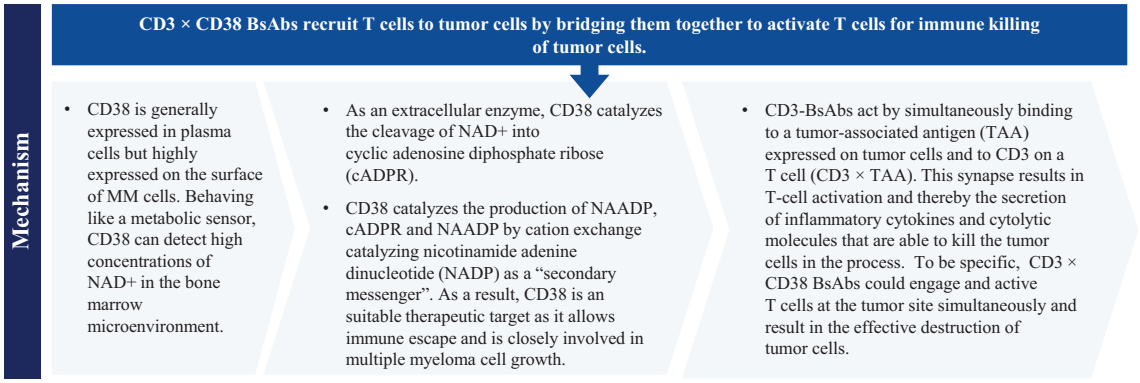
Despite of the continuous development of therapies to treat MA and MPE, there remain medical demands for innovative treatment options, mainly due to the following: (a) the distinct disadvantages of current treatments for MA and MPE, including causing significant patient discomfort and risks, and diminishing efficacy with tumor progression; (b) the lack of standard treatment guideline for MA globally and in China. Different guidelines have different mechanisms on the management of MA, and relevant studies have shown significant heterogeneity in the quality, recommendations and level of evidence among different treatment guidelines, and even within the same guidelines. Therefore, the current treatment options could not meet the demands of the patients, and a standard treatment with proven efficacy and favorable safety profile is desired by the market; and (c) MPE, as an aggressive disease, is not curable for most MPE patients; therefore, the aim of treatment for MPE is mainly palliative. Further, MPE has a uniformly fatal prognosis and a life expectancy of only three to twelve months, and currently most of the drugs for MA and MPE can only relieve symptoms but are rarely effective in increasing survival rate. The development of an effective targeted therapy is therefore desired by the patients.

CD38 × CD3 Targeted BsAbs

Mechanisms of CD38 × CD3 Targeted BsAbs

The CD38 antigen is highly and uniformly expressed on plasma cells and therefore represents an ideal target for the treatment of multiple myeloma with anti-CD38 mAbs. A CD38 × CD3 BsAb is designed to bind both CD38 on target MM tumor cells and CD3 on T cells, allowing activated T cells to attack target tumor cells. When compared with mAb products with the same target, the CD38 × CD3 BsAb has the advantages of better efficacy, less likely to

develop drug resistance and smaller dosage. The expected effective dose of the CD38 × CD3 BsAb is 1/20 of that of mAbs, which can significantly reduce drug costs and improve the quality of patients' survival. The following diagram illustrates the mechanism of action of the CD38 × CD3 BsAbs.



Source: Medicina, 2019, 55(8): 490., Cellular and Molecular Life Sciences, 2018, 75(3): 509-525., Cancer treatment reviews, 2010, 36(6): 458-467., International journal of cancer, 2014, 135(11): 2623-2632., Blood, The Journal of the American Society of Hematology, 2001, 98(8): 2526-2534., Frost & Sullivan Analysis

Multiple Myeloma (MM)

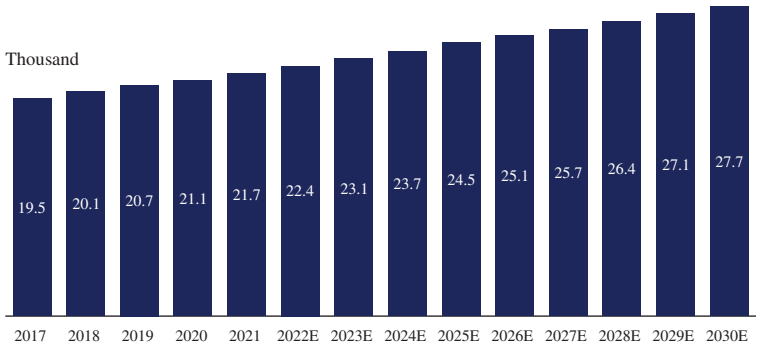
MM is a cancer of the plasma cells in the bone marrow. Plasma cells are antibody-producing white blood cells that are critical to the immune system. Myeloma begins when healthy plasma cells become cancerous and grow out of control. MM often results in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures.

The prognosis of a MM patient is very heterogeneous and is subject to various factors, such as genetics, performance status and stage of disease, which in turn determine the treatment and management of the disease. Current treatment regimens can prolong patient survival only and patients will eventually relapse and succumb to their disease. For most of the patients, MM will eventually develop into rrMM. This makes patients require continuous treatment in order to manage MM as a chronic disease and prefer treatment regimens with convenient administration. Existing treatment options with different mechanisms of action are usually exhausted early on in the treatment, as patients are treated with doublet and triplet combination regimens in early treatment lines. Therefore, new classes of therapy with innovative mechanisms of action are required for patients that relapse or are refractory to the current classes of drugs.

As illustrated in the diagram below, the annual incidence of MM in China has grown from 19.5 thousand in 2017 to 21.7 thousand in 2021, representing a CAGR of 2.7%. It is expected that the prevalence will increase to 24.5 thousand in 2025 and 27.7 thousand in 2030 at a CAGR of 3.1% and 2.5% from 2021 to 2025 and from 2025 to 2030, respectively.

China's Incidence of MM, 2017-2030E

Period	CAGR
2017-2021	2.7%
2021-2025E	3.1%
2025E-2030E	2.5%



Source: NCCR, Frost & Sullivan

According to Frost & Sullivan, the addressable rrMM patients of Y150 in China in 2030 is estimated to be 60.4 thousand. The table below sets forth the basis and assumption of the estimation of Frost & Sullivan.

Addressable rrMM Patients of Y150 in China	Unit	2030E
Incidence of MM[(1)]	Thousand	27.7
rrMM Prevalence[(2)]	Thousand	84.4
Treatment Rate[(3)]	%	85.8
2nd-Line Treatment Rate[(4)]	%	83.5
Addressable Patients[(5)]	**Thousand**	**60.4**

Notes:

(1) The source of MM incidences in China are National Cancer Registry and International Agency for Research on Cancer.

(2) The prevalence of rrMM is calculated by accumulating the number of MM patients who progress to rrMM over the years and subtracting the number of deceased patients from that population. According to the Second China Hematology Development Conference, almost all MM patients will eventually relapse, and the 5-year recurrence rate of MM is nearly 70%.

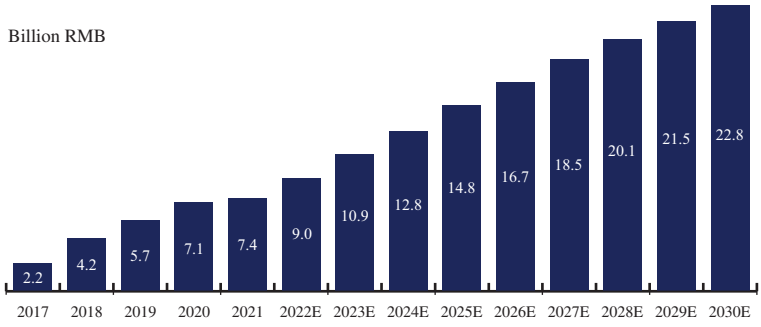
(3) The 1st-line treatment rate and 2nd-line treatment rate of rrMM are around 85.8% and 83.5%, respectively.

(4) The addressable rrMM patients for Y150 are those who are undergoing 2nd or later-lines of treatment for rrMM. In this table, the number of addressable patients (60.4 thousand) is arrived by multiply the rrMM Prevalence by the Treatment Rate and 2nd-Line Treatment Rate (84.4 thousand * 85.8% * 83.5%).

The market size of MM therapies grew from RMB2.2 billion in 2017 to RMB7.4 billion in 2021, representing a CAGR of 35.2%. It is predicted that the number will continue to grow, and reach RMB14.8 billion in 2025, RMB22.8 billion in 2030, with CAGR of 19.0% and 9.1% from 2021 to 2025 and from 2025 to 2030, respectively.

China's Market Size of MM Therapies, 2017-2030E

Period	CAGR
2017-2021	35.2%
2021-2025E	19.0%
2025E-2030E	9.1%



Source: Annual Reports of Listed Medical Companies, NCCR, MOHRSS, Frost & Sullivan Analysis

Competitive Landscape of CD38 Targeted Therapies

CD38 is an emerging target for the treatment of MM. There are multiple CD38 targeted antibodies being developed for the treatment of MM. The following table sets forth the details of marketed CD38 targeted antibody drugs or fusion proteins for the treatment of MM globally (excluding China) and in China as of the Latest Practicable Date:

Global Marketed Drugs

Product	Drug Name	Developer	Target	Drug Type	Indication	Approval Date	Price (USD)	Combination Therapy
DARZALEX FASPRO	Daratumumab	Genmab A/S	CD38	mAb	MM	May 1, 2020	1800mg/15ml 15ml: 9,611	Combination with lenalidomide/ bortezomib and dexamethasone
SARCLISA	Isatuximab	Sanofi	CD38	mAb	MM	March 2, 2020	20mg/ml 5ml: 783	Combination with carfilzomib and dexamethasone
DARZALEX	Daratumumab	Genmab A/S	CD38	mAb	MM	November 16, 2015	20mg/ml 5ml: 713	Combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant

Global Marketed Drugs

Product	Drug Name	Developer	Target	Drug Type	Indications	Approval Date	Price (RMB) in 2021	Combination Therapy
DARZALEX	Daretuzumab Injection	Janssen-Cilag International NV	CD38	mAb	MM	July 4, 2019	100mg: 2,358	Combination with lenalidomide/ bortezomib and dexamethasone

Source: NMPA, CDE, FDA, NKEXnews, Annual Reports of Listed Medical Companies, NRDL, Clinical Trials, Frost & Sullivan

As of the Latest Practicable Date, there were 22 and nine CD38 targeted antibody drug candidates or fusion proteins for the treatment of MM under clinical development globally (excluding China) and in China, respectively.

The development of CD38 targeted BsAb is still at its emerging stage. However, there is no evidence that BsAbs offer any significant clinical advantages compared to fusion proteins. For a comparative analysis of BsAb and fusion protein, please refer to the paragraphs headed "– Global and China Antibody Drug Market – Overview" in this section. The following table sets forth the competitive landscape of CD38 targeted BsAb for the treatment of MM globally as of the Latest Practicable Date:

Global Pipeline

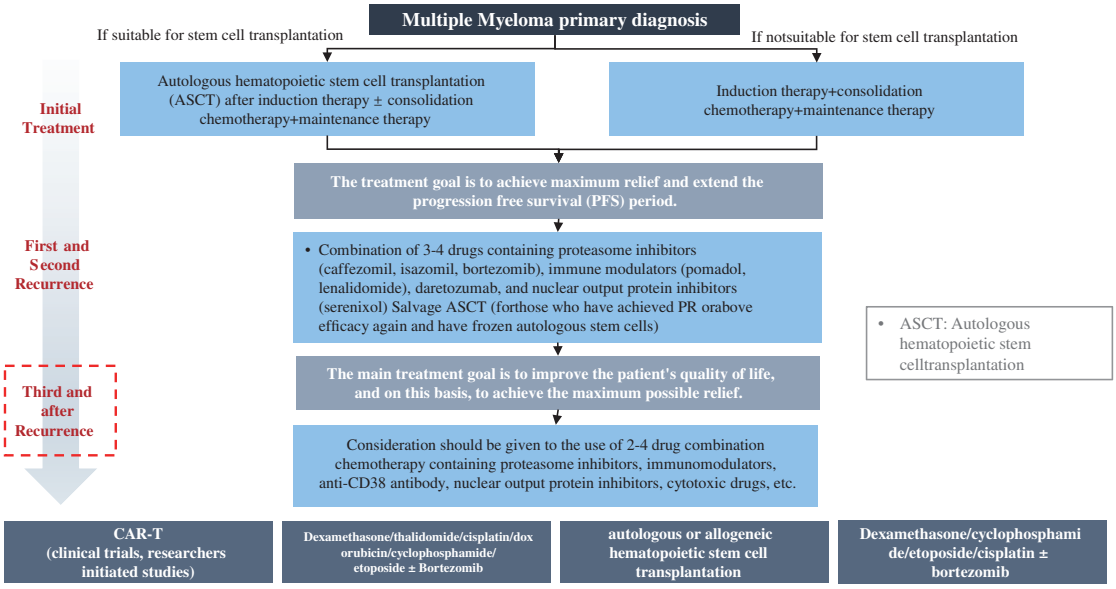
Product	Developer	Target	Drug Type	Indication	Highest Clinical Phase		First Posted Date[(1)]
Y150	the Company	CD38, CD3	BsAb	Multiple myeloma	Global	FDA IND Approval	\
					China	I	2021/5/28
ISB 1442	Ichnos Sciences SA	CD38, CD47	BsAb	Multiple myeloma	Global	I/II	2022/6/22
ISB 1342	Ichnos Sciences SA, Glenmark Pharmaceuticals S.A.	CD38, CD3	BsAb	Multiple myeloma	Global	I	2017/10/13
SG2501	Hangzhou Sumgen Biotech Co., Ltd.	CD38, CD47	BsAb	Relapsed or Refractory Hematological Malignancies and Lymphoma	Global	I	2022/3/24

Source: NMPA, CDE, ClinicalTrial.gov, FDA, Frost & Sullivan Analysis

(1) "First Posted Date" in terms of global clinical trials refers to the date when the study corresponding to the global highest clinical phase (except China) was first available on ClinicalTrials.gov after the National Library of Medicine has concluded its quality control review; "First Posted Date" in the context of China clinical trials refers to the date when the study corresponding to the highest clinical phase in China was first available on chinadrugtrials.org.cn after the Center for Drug Evaluation (CDE) has concluded its review. The CDE is an affiliated institution of the NMPA.

The development of CD38 targeted therapy in combination with other drugs represents a validated therapeutic strategy. For instance, the results of the Phase I/II clinical trial of daratumumab, a marketed CD38 targeted drug, for rrMM treatment, indicated the efficacy of monotherapy in patients with heavily pretreated rrMM. Moreover, in a Phase I/II clinical trial and a Phase III clinical trial of the combination therapy involving CD38 targeted drugs (daratumumab) for rrMM treatment, daratumumab in combination with lenalidomide/dexamethasone showed encouraging efficacy in patients with rrMM. The results of such clinical trials also indicated that the combination of CD38 targeted drugs and lenalidomide may have better efficacy than CD38 targeted monotherapies, evidencing the potentials of CD38 targeted BsAbs, including Y150, in combination therapies for rrMM treatment.

Treatment Paradigm for MM in China



Intended position and clinical focus of the Company's drug candidate

Source: CMDA, Frost & Sullivan analysis

The following table sets forth features and limitations of treatments for rrMM patients.

Major Treatments	Features	Limitations
Anti-CD38 Antibody+PIs + IMiDs	Studies showed the combination of daratumumab, lenalidomide, and dexamethasone showed better efficacy than other regimens in terms of nonresponse rate (NRR), time to progression (TTP), progression-free survival (PFS)	Infusion-related reactions still haven't been solved and more combined strategies are needed to maximize the strength of CD38 in the treatment of rrMM. CD38 antibodies do not clear small residual lesions (MRD) and patients remain vulnerable to relapse and drug resistance.
PIs + Chemotherapy	The proteasome degrades proteins through the ubiquitin-proteasome system (UPS). Due to the genetic instability and rapid proliferation of MM cells, it relies more on the proteasome to remove misfolded or damaged proteins .	Different proteasome inhibitors (PIs) have different mechanisms of action, and also cause different adverse drug reactions in the process of anti-MM
IMiDs + Chemotherapy	IMiD has direct and indirect anti-tumor effects. On the one hand, IMiD can directly induce cell cycle arrest and apoptosis in myeloma cells; on the other hand, immunomodulatory drugs (IMiDs)'s indirect anti-myeloma activity is through changing the It is mainly related to IMiD inhibiting the expression of surface adhesion molecules on MM cells and bone marrow stromal cells (BMSCs) and inhibiting angiogenesis	With the popularization of IMiD in the treatment of MM, its drug resistance has gradually emerged, which makes the treatment of MM encounter difficulties again.
CAR-T	MM is difficult to cure, and recurrence and refractory remain major problems in MM treatment. Multiple clinical studies have shown that CAR-T therapy targeting B-cell maturation antigen (BCMA) improves remission rates in relapsed refractory MM	At present, autologous T cell "modification" is the main technology of CAR-T, that is, the patient's own T cells are extracted for gene editing and then infused. The treatment process is notonly time-consuming and expensive, but also has a high risk of CRS. In addition, the patients often receive a multiple of treatments in the early stage, and their immune cells are severely weakened, which limits its clinical efficacy.
BCMA x CD3 BsAb	Antibodies against cellular adhesion molecules such as B Cell Maturation Antigen (BCMA), such as Teclistamab, can serve as a bridge between T cells and Plasma tumor cells expressing BCMA, leading to T cell activation and subsequent killing of the tumor cells. Teclistamab can be utilized to treat patients with rrMM who have not responded to CD38, PIs, and IMiDs treatments.	Teclistamab was approved by the FDA based on a Phase II clinical trial involving only 110 patients. However, further clinical efficacy data and safety profiles are required to fully establish its efficacy and safety in treating multiple myeloma.

Intended position and clinical focus of the Company's drug candidate

Abbreviations: PIs refers to Protease inhibitor, a class of compounds that inhibit the activity of protein kinases; IMiD refers to immunomodulatory drug, drug that regulate cellular and humoral immune functions and can enhance immune function, such as Lenalidomide.

Future Trends and Needs of MM Treatment

The future trends of MM treatment mainly include: (a) strategies that focus more on the continued improvement in long-term outcomes of emerging pipeline therapies, along with the combination of newer agents with establish regimens; (b) developing indicators that can predict different treatment responses and different prognoses of patients, since MM is incurable, patients will eventually relapse and require further treatment, and the discovery of indicators that can distinguish patients with good prognosis from patients with poor prognosis will facilitate the guidance of treatment options for patients; and (c) the clinical focus on overcoming drug resistance, which the basis for disease relapse in most patients.

Despite of the continuous development of therapies to address the demands of MM patients, there remain medical demands, including the following: (a) MM remains incurable and patients will eventually relapse and succumb to their disease; therefore, patients may require continuous treatment in order to manage MM, and new classes of therapy with novel mechanisms of action are required for patients that relapse or are refractory to the current classes of drugs; and (b) the significant cost of treatment for MM patients lead to strong demands for more cost-effective therapies.

HER2 × CD3 Targeted BsAb

Mechanisms of HER2 × CD3 Targeted BsAbs

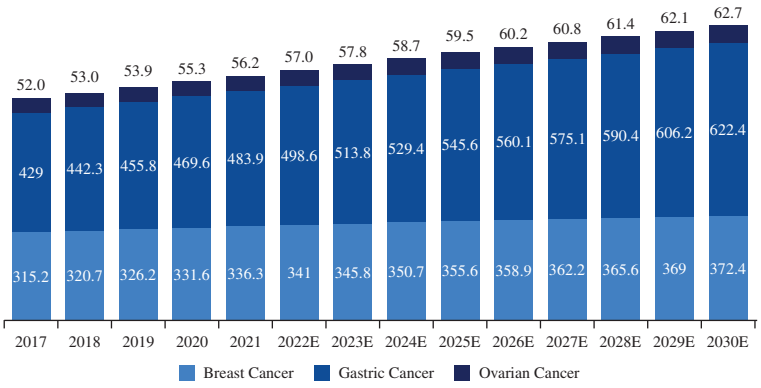
HER2 is a ligand-orphan receptor which is expressed in many human tumors, especially in breast cancers. An anti-HER2 × CD3 BsAb recruits and redirects T cells to HER2+ tumor cells through binding to CD3 and HER2, and further activates T cells to kill the tumor cells. Additionally, the anti-HER2 × anti-CD3 BsAb prevents the dimerization of the receptor HER2, increases endocytic destruction of the receptor, and inhibits shedding of the extracellular domain of HER2.

Market of HER2 Targeted BsAb

HER2 is highly expressive in many types of cancers, including breast cancer, gastric cancer and ovarian cancer. The incidence of breast cancer, gastric cancer and ovarian cancer in China reached 336.3 thousand, 483.9 thousand and 56.2 thousand in 2021, respectively, and is expected to reach 355.6 thousand, 545.6 thousand and 59.5 thousand in 2025 and 372.4 thousand, 622.4 thousand and 62.7 thousand in 2030, respectively. In particular, the annual incidence of late-stage HER2 positive gastric cancer and late-stage HER2 positive breast cancer are expected to reach 109.5 thousand and 49.9 thousand, respectively, in China by 2030.

China's Incidence of Breast Cancer, Gastric Cancer and Ovarian Cancer, 2017-2030E

CAGR	Breast Cancer	Gastric Cancer	Ovarian Cancer
2017-2021	1.6%	3.1%	2.0%
2021-2025E	1.4%	3.0%	1.4%
2025E-2030E	0.9%	2.7%	1.1%



Source: NCCR, Frost & Sullivan Analysis

(1) the epidemiological data for cancer in this stacked graph are non-accumulative

According to Frost & Sullivan, the addressable breast cancer patients of M802 in China in 2030 is estimated to be 13.6 thousand. The table below sets forth the basis and assumption of the estimation of Frost & Sullivan.

Addressable Breast Cancer patients of M802 in China	Unit	2030E
Breast Cancer Incidence[(1)]	Thousand	372.4
Total Late Stage HER2+ Breast Cancer Patients[(2)]	Thousand	49.9
Treatment Rate[(3)]	%	95.0
2nd-line Treatment Rate[(4)]	%	60.0
3rd-line Treatment Rate[(5)]	%	48.0
Addressable patients[(6)]	**Thousand**	**13.6**

Notes:

(1) The source of breast cancer incidences in China is National Cancer Registry and International Agency for Research on Cancer.

(2) The total number of late-stage HER2+ breast cancer patients are calculated by taking the breast cancer incidence and multiplying it by the proportion of late-stage breast cancer patients (52.8%, according to published research paper). Then, add the number of non-late-stage breast cancer patients multiplied by the proportion of non-late-stage breast cancer patients who progress to late-stage breast cancer (30%, according to the China Guidelines for Standardized Diagnosis and Treatment of Advanced Breast Cancer). Finally, multiply the result by the proportion of HER2+ breast cancer patients (20%, according to published research paper). In summary, the 49.9 thousand is derived from the below formulation: (372.4 thousand * 52.8% + (372.4 thousand * (1-52.8%) * 30%)) * 20%.

(3) Nearly all patients are willing to undergo treatment when they are first diagnosed with breast cancer, with a treatment rate of around 95%.

(4) The treatment rate for the 1st line is relatively high, while the treatment rate for the subsequent lines of treatment is comparatively lower.

(5) The 3rd-line treatment rate for breast cancer is expected to be around 48% by 2030.

(6) The addressable breast cancer patients for M802 are those who are undergoing 3rd-line treatment or later lines of treatment for HER2+ breast cancer. In this table, the number of addressable patients (13.6 thousand) is arrived by multiply the Total Late Stage HER2+ Breast Cancer Patients by the Treatment Rate, 2nd-line Treatment Rate and 3rd-line Treatment Rate (49.9 thousand * 95.0% * 60.0% * 48.0%).

According to Frost & Sullivan, the addressable gastric cancer patients of M802 in China in 2030 is estimated to be 39.4 thousand. The table below sets forth the basis and assumption of the estimation of Frost & Sullivan.

Addressable Gastric Cancer Patients of M802 in China	Unit	2030E
Gastric Cancer Incidence[(1)]	Thousand	622.4
Total Late Stage HER2+ Gastric Cancer Patients[(2)]	Thousand	109.5
Treatment Rate[(3)]	%	95.0
2nd-line Treatment Rate[(4)]	%	62.1
3rd-line Treatment Rate[(5)]	%	61.0
Addressable patients[(6)]	**Thousand**	**39.4**

Notes:

(1) The source of gastric cancer incidences in China is National Cancer Registry and International Agency for Research on Cancer.

(2) The total number of late-stage HER2+ gastric cancer patients are calculated by taking the gastric cancer incidence and multiplying it by the proportion of late-stage gastric cancer patients (80%, according to published research paper). Then, add the number of non-late-stage gastric cancer patients multiplied by the proportion of non-late-stage gastric cancer patients who progress to late-stage gastric cancer (40%, according to published research paper). Finally, multiply the result by the proportion of HER2+ gastric cancer patients (20%, according to published research papers). In summary, the 109.5 thousand is derived from the below formulation: (622.4 thousand * 80% + (622.4 thousand * (1-80%) * 40%)) * 20%.

(3) Nearly all patients are willing to undergo treatment when they are first diagnosed with gastric cancer, with a treatment rate of around 95%.

(4) The treatment rate for the 1st line is relatively high, while the treatment rate for the subsequent lines of treatment is comparatively lower.

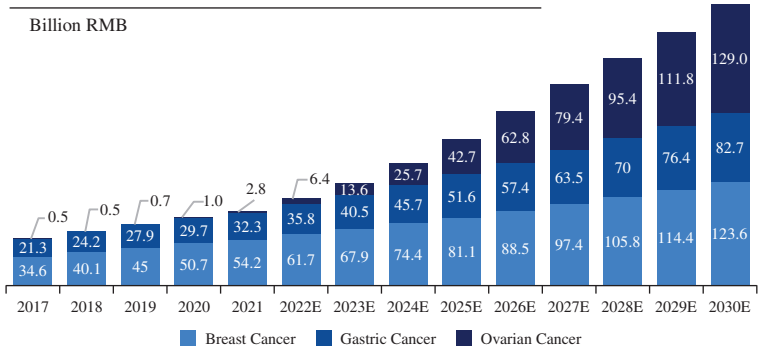
(5) According to published research paper, the 3rd-line treatment rate for gastric cancer is approximately 61%.

(6) The addressable gastric cancer patients for M802 are those who are undergoing 3rd-line treatment or later lines of treatment for HER2+ gastric cancer. In this table, the number of addressable patients (39.4 thousand) is arrived by multiply the Total Late Stage HER2+ Gastric Cancer Patients by the Treatment Rate, 2nd-line Treatment Rate and 3rd-line Treatment Rate (109.5 * 95.0% * 62.1% * 61.0%)

The market size of breast cancer, gastric cancer and ovarian cancer in China reached RMB54.2 billion, RMB32.3 billion and RMB2.8 billion in 2021, respectively, and is expected to reach 81.1 thousand, 51.6 thousand and 42.7 thousand in 2025 and RMB123.6 billion, 82.7 billion and RMB129.0 billion in 2030, respectively.

China Market Size of Breast Cancer, Gastric Cancer and Ovarian Cancer, 2017-2030E

CAGR	Breast Cancer	Gastric Cancer	Ovarian Cancer
2017-2021	11.9%	11.0%	57.2%
2021-2025E	10.6%	12.4%	97.1%
2025E-2030E	8.8%	9.9%	24.8%



Source: Annual Reports of Listed Medical Companies, NCCR, MOHRSS, Frost & Sullivan Analysis

(1) the market size data for cancer in this stacked graph are non-accumulative

Competitive Landscape of HER2 Targeted Therapies

HER2 is an emerging target for cancer treatment. As of the Latest Practicable Date, there were 13 HER2 targeted antibody drugs approved for the treatment of HER2-positive solid tumors globally (excluding China), at price ranging from US$1,284 per dose to US$8,929 per dose, and five approved in China. As of the same date, there were 141 and 56 HER2 targeted antibody drug candidates or fusion proteins for the treatment of HER2-positive solid tumors under clinical development globally (excluding China) and in China, respectively. The following table sets forth the details of marketed HER2 targeted antibody drugs or fusion proteins for the treatment of HER2-positive solid tumors in China as of the Latest Practicable Date:

China Marketed Drugs

Product	Drug Name	Developer	Target	Drug Type	Indications	Approval Date	Price (RMB) in 2021	Combination Therapy
Herceptin	Trastuzumab for Injection	Roche Pharma	HER2	mAb	Gastric Cancer, Breast Cancer, and HER2-positive Breast Cancer	October 22, 2021	440mg: 5,500	Combination with trastuzumab
Zercepac	Trastuzumab Injection	Shanghai Henlius Biotech, Inc.	HER2	mAb	Gastric Cancer, Breast Cancer, and HER2-positive Breast Cancer	August 12, 2020	150mg: 1,688	Combination with pertuzumab
Cipterbin	Inetetamab for Injection	Sunshine Guojian Pharmaceutical (Shanghai) Co., Ltd.	HER2	mAb	HER2-positive Breast Cancer	June 17, 2020	50mg: 590	Combination with chemotherapy
Kadcyla	Trastuzumab Emtansine for Injection	Roche Pharma (Schweiz) AG	HER2	ADC	HER2-positive Breast Cancer	January 21, 2020	100mg: 19,282	Purple shingles in combination with trastuzumab-based neoadjuvant therapy
Perjeta	Pertuzumab Injection	Roche Pharma (Schweiz) AG	HER2	mAb	HER2-positive Breast Cancer	December 17, 2018	420mg: 4,955	Combination with pertuzumab
Enhertu	Dextrastuzumab for injection	DAIICHI SANKYO COMPANY	HER2	ADC	HER2 positive breast cancer	February 21, 2023	100mg: 9,432	NA
HS022	Trastuzumab for injection	Hisun Biopharmaceutical Co., Ltd.	HER2	mab	Breast cancer, Gastric cancer	February 28, 2023	150mg:1,588	Combination with vinorelbine
RC48	Disitamab Vedotin for injection	Remegen Co., Ltd.	HER2	ADC	Urothelial carcinoma, gastric carcinoma, gastroesophageal junction adenocarcinoma	June 8, 2021	60mg:13,500	Combination with toripalimab

Source: NMPA, CDE, NKEXnews, Annual Reports of Listed Medical Companies, NRDL, Frost & Sullivan

As of the Latest Practicable Date, there were ten HER2-targeted BsAb pipelines under clinical development globally (excluding China), and 13 HER2-targeted BsAb pipelines under clinical development in China. The development of HER2 × CD3 BsAbs represents an emerging trend. As of the Latest Practicable Date, there were four HER2 × CD3 BsAbs under clinical development globally, including M802, RG6194, EX 101 Injection and AMX 818, as illustrated in the table below:

Product	Developer	Target	Drug Type	Indication	Highest Clinical Phase		First Posted Date[(1)]
Runimotamab (RG6194)	Genentech, Inc.	HER2, CD3	BsAb	Advanced or Metastatic HER2-Expressing Cancers	Global	I	2018/2/27
M802	the Company	HER2, CD3	BsAb	Advanced HER2-Expressing Solid Tumors	Global China	FDA IND Approval I	\ 2018/7/26
EX101 Injection	Guangzhou AI Simai Biomedical Technology Co., Ltd.	HER2, CD3	BsAb	HER2-positive advanced solid tumors	China	I	2021/09/15
AMX 818	Amunix Pharmaceuticals	HER2, CD3	BsAb	Locally Advanced or Metastatic HER2-Expressing Cancers	Global	I	2022/5/2

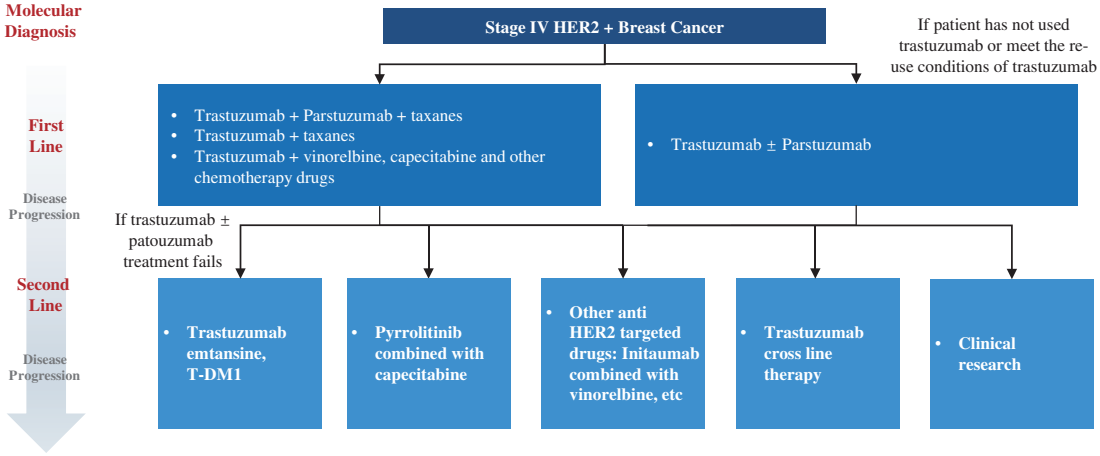
Source: CDE, Frost & Sullivan Analysis

(1) "First Posted Date" in terms of global clinical trials refers to the date when the study corresponding to the global highest clinical phase (except China) was first available on ClinicalTrials.gov after the National Library of Medicine has concluded its quality control review; "First Posted Date" in the context of China clinical trials refers to the date when the study corresponding to the highest clinical phase in China was first available on chinadrugtrials.org.cn after the Center for Drug Evaluation (CDE) has concluded its review. The CDE is an affiliated institution of the NMPA.

The development of HER2 x CD3 BsAb represents a validated therapeutic strategy. For instance, the results of Phase I clinical trial of Ertumaxomab, a HER2 × CD3 targeted BsAb, for metastatic breast cancer showed encouraging anti-tumor efficacy, evidencing the therapeutic potential of HER2 × CD3 targeted BsAb, including M802, in treating HER2-positive solid tumors.

Treatment Paradigm for Breast Cancer in China

M802 is an innovative therapy intended for the treatment of HER2+ late-stage breast cancer patients in the third-line and beyond where there is no treatment guideline. M802 is therefore not currently included in the treatment paradigm below.



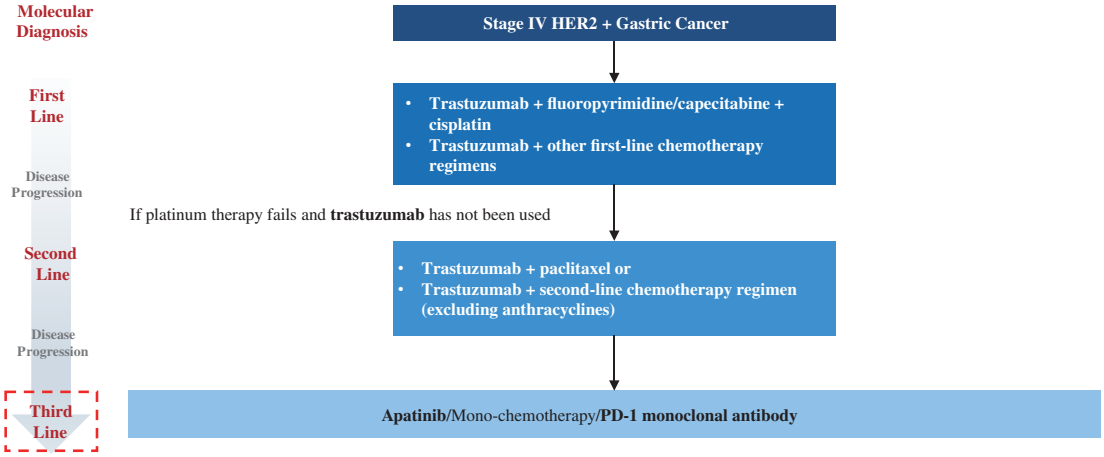
Source: NHC, Frost & Sullivan Analysis

The following table sets forth features and limitations of 2L/2L+ treatments for late stage HER2+ breast cancer patients.

Treatment	Features	Limitations
Chemotheropy + Anti-HER2 antibodies	1.significantly improved the median progression-free survival (PFS) 2.These antibodies mainly inhibit tumor growth by blocking the signaling pathways associated with tumor cell growth, or killing tumor cells through antibody-mediated effects such as ADCC.	A greater proportion of patients with low HER2 expression do not have good access to HER2-targeted therapies; a higher proportion of patients with high HER2 expression still do not respond to HER2-targeted therapies; HER2-targeted therapies of the same mechanism may gain the sameresistant after a period of time.
Chemotheropy + Anti-HER2 antibodies+TKI	1.Higher specificity than monotherapy 2.Reducing drug resistance using the differentanti-tumor mechanisms between antibodies and TKI.	Some patients may not tolerate combination therapy. Adverse events(AEs) possibly happen. In addition, now it is mainly effective for high expression of HER2 and more than half of patients with high expression of HER2 are still ineffective. Drug resistance maydevelop quickly after treatment, and other new mechanisms to improve the efficacy of this therapy still need to be developed.
Chemothropy + TKI	Oral dosage forms are convenient to use, and help to improve patient compliance. Small molecule drugs can cross the blood-brain barrier, which shows excellent efficacy in patients with brain metastases	Requires long-term medication, which affects the patient's quality of life. Resistance develops relatively quickly after treatment, and other new mechanisms of therapy are still needed.
Anti-HER2 ADC	ADC links a humanized monoclonal antibody targeting a specific antigen on the surface of tumor cells with cytotoxic agent into cancer cells, reducing systemic exposure of thecytotoxic agents compared to the conventional chemotherapy.	The cysotoxin causesby off-target toxicity of ADC or other chemotherapy-associated AEs (adverse events). Resistance can also develop relatively quickly after treatment.

Intended position and clinical focus of the Company's drug candidate

Treatment Paradigm for Gastric Cancer in China



Intended position and clinical focus of the Company's drug candidate

Source: National Health Commission of the People's Republic of China, Frost & Sullivan Analysis

M802 is intended for the treatment of HER2+ late-stage gastric cancer patients in the third-line and beyond where there is no treatment guideline. M802 is therefore not currently included in the treatment paradigm above.

The following table sets forth features and limitations of 2L/2L+ treatment for late stage HER2+ gastric cancer patients.

Treatment	Features	Limitations
Anti-VEGF antibody (e.g. Ramucirumab)+chemo (e.g. paclitaxel)	Improved survival prognosis foradvanced gastric cancer indicating overall survival (OS) and progression-free survival (PFS)	Limited efficacy, Ramucirumab not available in China at present. Treatment-related AEs (TRAEs) of any grade that occurred in at least 10% of the patients.
TKI (e.g.Apatinib)	It is efficient for patients with gastric cancer who have failed second-line chemotherapy or higher. Study showed that apatinib mesylate treatment prolonged median PFS and improved disease control rate	Limited efficacy. Combination therapy with chemotherapy does not improve its performance in the treatment of end-stage gastric cancer
Anti-PD-1 antibodies (e.g.Pembrolizumab)	A good performance as a 3L treatment in patients with progressive or metastatic gastric cancer.	Limited efficacy. Only good for 3L/3L+ treatment of patients whose previous treatment didn't include PD-1/PD-L1 monoclonal antibody
Anti-HER2 antibody (e.g. Trastuzumab)+chemo (e.g. taxol, anthracyclines)**	Several studies have shown that HER2 positivity was associated with poor prognosis and clinical characteristics in gastric cancer and anti-HER2 drugs are recommended for the first-line treatment in guidelines.	A greater proportion of patients with low HER2 expression do not have a good access to HER2-targeted therapies, a higher proportion of patients with high HER2 expression still do not respond to HER2-targeted therapies, and HER2-targeted therapies of the same mechanism may gain the same resistant after a period of time

Intended position and clinical focus of the Company's drug candidate

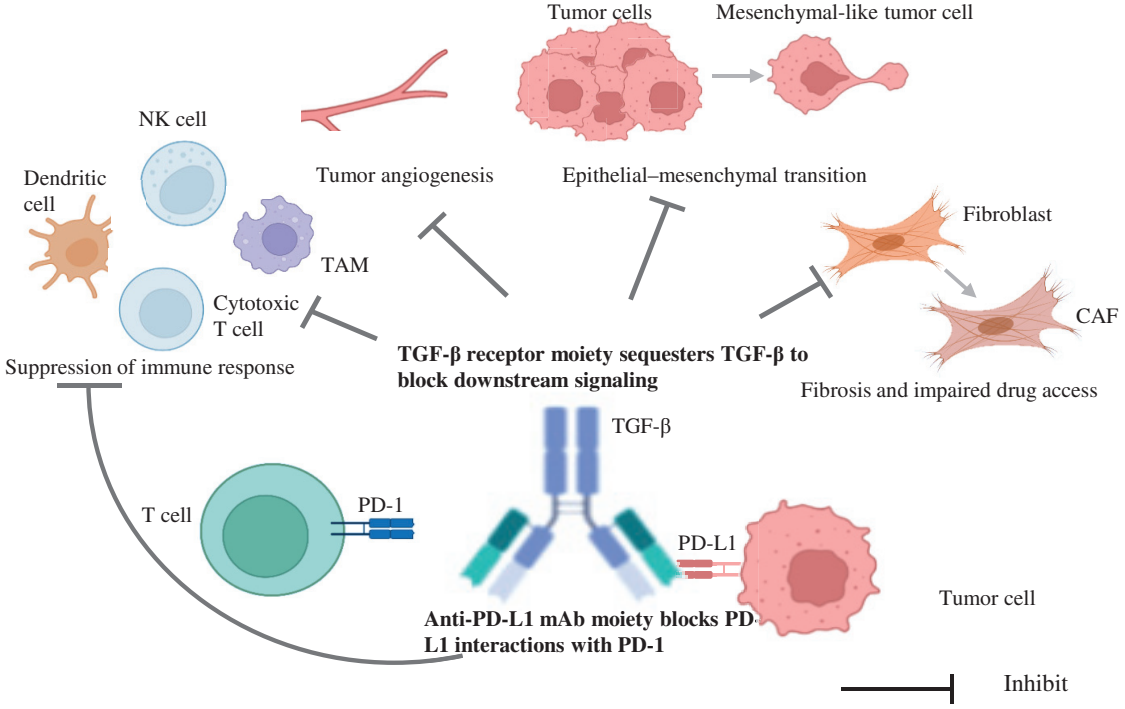
PD-1/PD-L1 × TGF-β TARGETED DRUGS MARKET

Anti-PD-1/PD-L1 Therapy and TGF-β Pathway

Programmed Death-1 (PD-1) is a critical immune checkout receptor expressed on T cells upon activation. Engagement of PD-1 by its ligands, PD-L1 and PD-L2, transduces a signal that inhibits T cell proliferation, cytokine production, and cytolytic function. The normal function of PD-1 is to modulate T cell-mediated immune response in order to prevent the immune system from attacking normal healthy tissue in the body. However, this safeguarding mechanism is often exploited by cancer cells to evade immune surveillance. Many solid tumor cells produce a large amount of PD-L1 to circumvent T cell assaults.

The transforming growth factor-β (TGF-β) is a family of structurally related proteins that has a dual action in cancer as a tumor suppressor and a tumor promoter. It can induce cellular growth arrest and apoptosis at the early stage of cancer as a tumor suppressor. During later stages of tumor progression, it acts as a tumor promoter and induce migration and stimulate epithelial to mesenchymal transition.

TGF-β can promote PD-1/PD-L1 resistance by converting conventional T cells to immune-suppressive T-reg cells and increasing the survival of myeloid progenitors that differentiate to potent myeloid-derived suppressor cells (MDSCs). Both of these processes result in increased expression of TGF-β while MDSCs express PD-L1 and drive T-reg cell differentiation. By simultaneously inhibiting the PD-1/PD-L1 axis and the TGF-β signaling pathways, a PD-1/PD-L1 × TGF-β targeted BsAb could restore the dysregulated anti-tumor immunity of cancer patients and establish an immuno-supportive tumor microenvironment. The diagram below illustrates the mechanism of action of PD-1/PD-L1 × TGF-β targeted BsAbs.



Source: Journal for ImmunoTherapy of Cancer, 2022, 10(12): e005543., Molecular oncology, 2022, 16(11): 2117-2134., Antibody Therapeutics, 2020, 3(2): 126-145., ADMET and DMPK, 2017, 5(3): 159-172., Frost & Sullivan Analysis

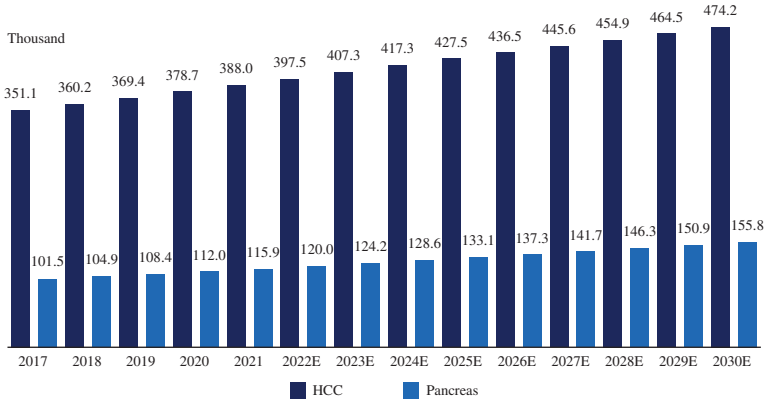
Abbreviations: TAM refers to Tumor-associated macrophage; CAF refers to Cancer-associated fibroblast.

China's Market of PD-1/PD-L1 × TGF-β Targeted Drugs

According to Frost & Sullivan, anti-PD-1/PD-L1 antibodies have robust and durable anti-cancer activities across several solid cancers, such as pancreatic cancer and HCC. From 2017 to 2021, the incidence of HCC had grown from 351.1 thousand in 2017 to 388.0 thousand in 2021, representing a CAGR of 2.5%. It is expected that the the incidence of HCC will increase to 427.5 thousand in 2025 and 474.2 thousand in 2030, at a CAGR of 2.5% from 2021 to 2025, and 2.1% from 2025 to 2030. In particular, the annual incidence of late-stage HCC is expected to reach 237.1 thousand in China by 2030. The incidence of pancreatic cancer in China grew from 101.5 thousand in 2017 to 115.9 thousand in 2021, representing a CAGR of 3.4%. It is expected that the prevalence will increase to 133.1 thousand in 2025, and 155.8 thousand in 2030, at a CAGR of 3.5% from 2021 to 2025, and 3.2% from 2025 to 2030. In particular, the annual incidence of late-stage PC is expected to reach 124.6 thousand in China in 2030.

China's Incidence of HCC and Pancreatic Cancer, 2017-2030E

CAGR	Hepatocellular Carcinoma (HCC)	Pancreatic Cancer (PC)
2017-2021	2.5%	3.4%
2021-2025E	2.5%	3.5%
2025E-2030E	2.1%	3.2%



Source: NCCR, Frost & Sullivan Analysis

According to Frost & Sullivan, the addressable HCC patients of Y101D in China in 2030 is estimated to be 222.9 thousand. The table below sets forth the basis and assumption of the estimation of Frost & Sullivan.

Addressable HCC Patients of Y101D in China	Unit	2030E
Incidence of HCC[(1)]	Thousand	474.2
Late Stage HCC Patients[(2)]	Thousand	237.1
1st-line Treatment Rate[(3)]	%	94.0
Addressable Patients[(4)]	**Thousand**	**222.9**

Notes:

(1) The source of HCC incidences in China is Globocan.

(2) According to published research papers, approximately 50% of HCC patients are late stage patients. The number of Late Stage HCC Patients is derived from multiple the Incidence of HCC (474.2 thousand) by 50%.

(3) Approximately 94% of late-stage HCC patients take treatment first time they are diagnosed with HCC.

(4) Addressable patients mean late stage HCC patients who receive 1st-line treatment are addressable patients for Y101D. In this table, the number of addressable patients (222.9 thousand) is arrived by multiply the Incidence of HCC by the 1st-line Treatment Rate (237.1 thousand * 94.0%).

According to Frost & Sullivan, the addressable pancreatic cancer patients of Y101D in China in 2030 is estimated to be 104.7 thousand. The table below sets forth the basis and assumption of the estimation of Frost & Sullivan.

Addressable Pancreatic Cancer Patients of Y101D in China	Unit	2030E
Incidence of Pancreatic Cancer[(1)]	Thousand	155.8
Late Stage Pancreatic Cancer Patients[(2)]	Thousand	124.6
1st-line Treatment Rate[(3)]	%	84.0
Addressable Patients[(4)]	**Thousand**	**104.7**

Notes:

(1) The source of pancreatic cancer incidences in China is Globocan.

(2) According to published research papers, approximately 80% of pancreatic cancer patients are late-stage patients beyond the stage of surgical resection when diagnosed. The number of Late Stage Pancreatic Cancer Patients is derived from multiple the Incidence of Pancreatic Cancer (155.8 thousand) by 80%.

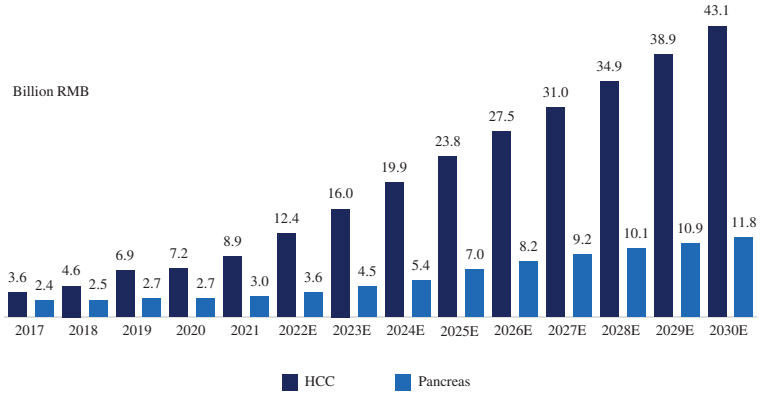
(3) The first-line treatment rate of late-stage pancreatic cancer patients is approximately 84%.

(4) Addressable patients mean late-stage pancreatic cancer patients who receive 1st-line treatment are addressable patients for Y101D. In this table, the number of addressable patients (104.7 thousand) is arrived by multiply the Incidence of Pancreatic Cancer by the 1st-line Treatment Rate (124.6 thousand thousand * 84.0%).

The market size of HCC in China has grown from RMB3.6 billion in 2017 to RMB8.9 billion in 2021, representing a CAGR of 25.4%. It is expected that the market size will increase to RMB23.8 billion in 2025, and RMB43.1 billion in 2030, at a CAGR of 27.9% and 12.6%, from 2021 to 2025 and from 2025 to 2030, respectively. The market size of pancreatic cancer in China has grown from RMB2.4 billion in 2017 to RMB3.0 billion in 2021, representing a CAGR of 6.5%. It is expected that the market size will increase to RMB7.0 billion in 2025, and RMB11.8 billion in 2030, at a CAGR of 23.1% and 11.1%, from 2021 to 2025 and from 2025 to 2030, respectively. The chart below illustrates China's market size of HCC and pancreatic cancer for the periods indicated.

China's Market Size of HCC and Pancreatic Cancer, 2017-2030E

CAGR	Hepatocellular Carcinoma (HCC)	Pancreatic Cancer (PC)
2017-2021	25.4%	6.5%
2021-2025E	27.9%	23.1%
2025E-2030E	12.6%	11.1%



Source: Annual Reports of Listed Medical Companies, NCCR, MOHRSS, Frost & Sullivan Analysis

Competitive Landscape of PD-1/PD-L1 × TGF-β Targeted Drugs

The PD-1/PD-L1-based pathway is of great value in immunotherapy of cancer and has become an important immune checkpoint during recent years. As of the Latest Practicable Date, there were 23 PD-1/PD-L1 targeted antibody drugs or fusion proteins approved for the treatment of solid tumors globally (excluding China), at price ranging from US$7,450 per dose to US$10,128 per dose, and 13 approved in China, at price ranging from RMB1,075 per dose to RMB32,800 per dose. These marketed products have proved the efficacy of PD-1/PD-L1 targeted pathway in tumor treatment. PD-1/PD-L1 targeted antibody drugs or fusion proteins can also be used in combination with other drugs, such as Bevacizumab, Lenvatinib, for the treatment of solid tumors.

More PD-1/PD-L1 targeted drug candidates for solid tumor treatment are under development. As of the Latest Practicable Date, there were 65 and 55 PD-1/PD-L1 targeted antibody drug candidates or fusion proteins for the treatment of solid tumors under clinical development globally (excluding China) and in China, respectively.

Considerable efforts have also been directed toward the studies of the TGF-β signaling pathway. As of the Latest Practicable Date, there was no TGF-β targeted antibody drug or fusion protein approved for the treatment of solid tumors globally. As of the same date, there were 20 and 16 TGF-β targeted antibody drugs or fusion proteins for the treatment of solid tumors under clinical development globally (excluding China) and in China, respectively.

Meanwhile, no PD-1/PD-L1 × TGF-β BsAb drug is marketed either globally or in China. There are 16 PD-1/PD-L1 × TGF-β targeted pipelines under clinical trials in China, among which Y101D is the only PD-L1 × TGF-β BsAb and the other 15 pipelines are PD-1/PD-L1 × TGF-β targeted bifunctional antibody-receptor fusion proteins. There is no evidence that BsAbs offer any significant clinical advantages compared to fusion proteins. For a comparative analysis between BsAb and fusion protein, please refer to the paragraphs headed "Industry Overview – Global and China Antibody Drug Market – Overview" in this document.

The following table summarizes the status of PD-1/PD-L1 × TGF-β pipelines under clinical trials in China as of the Latest Practicable Date:

China Pipeline

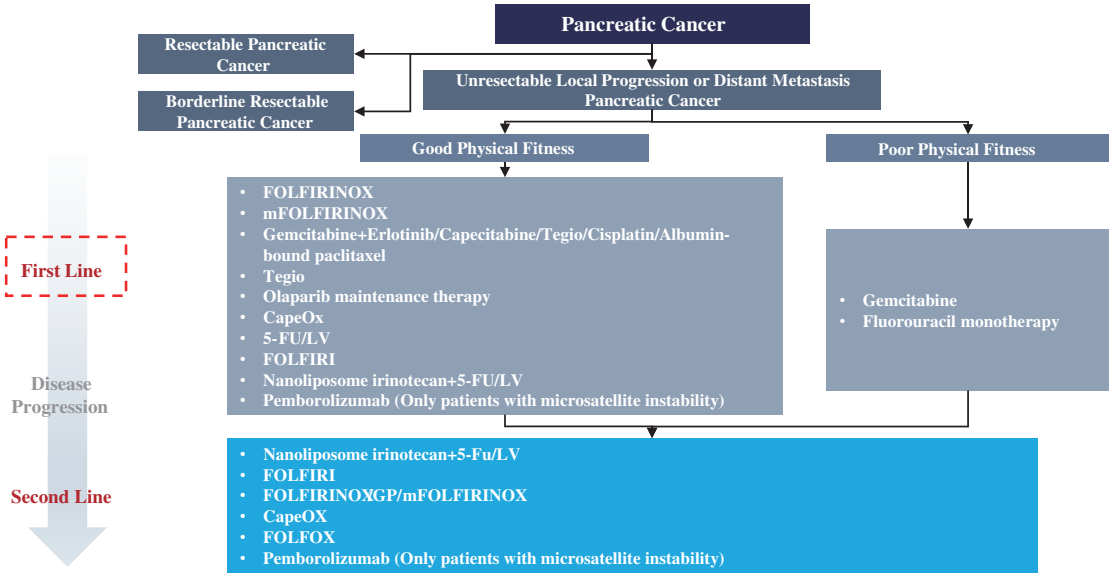
Product	Developer	Target	Drug Type	Indication	Highest Clinical Phase	First Posted Date(1)
M7824	Merck & Co., Inc.	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor (including, NSCLC, cholangiocarcinoma, cervical cancer)	III	2022/4/21
SHR-1701	Jiangsu Hengrui Medicine Co Ltd, Shanghai Hengrui Pharmaceutical Co Ltd, Suzhou Suncadia Biopharmaceuticals Co Ltd	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor (including, NSCLC, cervical cancer, gastric cancer)	III	2021/11/17
PM-8001	Biotheus Inc	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor	II	2020/6/24
TQB2858	Nanjing Jun Xin Pharmaceutical Co., Ltd.	PD-L1, TGF-β	Fusion Protein	Advanced malignant tumor	I	2021/3/25
JS-201	Shanghai Junshi Biosciences Co Ltd	PD-1, TGF-β	Fusion Protein	Advanced solid tumor	I	2021/5/21
QLS31901	Qilu Pharmaceutical Co., Ltd.	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor	I	2021/6/2
Y101D	the Company	PD-L1, TGF-β	BsAb	Metastatic or locally advanced solid tumors; HCC; PC	Ib/II	2022/12/05
BR102	Hisun Biopharmaceutical Co., Ltd.	PD-L1, TGF-β	Fusion Protein	Advanced malignant tumor	I	2021/9/13
LBL-015	Nanjing Leads Biolabs Co., Ltd.	PD-1, TGF-β	Fusion Protein	Advanced solid tumor	I	2021/9/22
TQB-2868	Nanjing Shunxin Pharmaceuticals Co, Ltd of Chiatai Tianqing Pharmaceutical Group	PD-1, TGF-β	Fusion Protein	Advanced malignant tumor	I	2022/2/14
BJ-005	Boji Biomedical Technology (Hangzhou) Co Ltd	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor; advanced lymphadenoma	I	2022/3/9
GT-90008	Kintor Pharmaceutical (Guangdong) Co., Ltd.	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor	I	2022/5/31
TST-005	Mabspace Biosciences (Suzhou) Co, Limited	PD-L1, TGF-β	Fusion Protein	Metastatic or locally advanced solid tumors (e.g. HPV positive, NSCLC)	I	2022/7/1
HB-0028	Huabo Biopharm Co Ltd	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor	I	2022/8/9
LY01019	Shandong Boan Biotechnology Co. Ltd	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor	I	2022/8/30
6MW3511	Mabwell (Shanghai) Bioscience Co., Ltd.	PD-L1, TGF-β	Fusion Protein	Advanced solid tumor	I	2022/9/1

Source: NMPA, CDE, Frost & Sullivan Analysis

(1) "First Posted Date" in the context of China clinical trials refers to the date when the study corresponding to the highest clinical phase in China was first available on chinadrugtrials.org.cn after the Center for Drug Evaluation (CDE) has concluded its review. The CDE is an affiliated institution of the NMPA.

Fusion protein refers to antibody fusion protein (Ig fusion protein), which is a bio-engineered protein that joins the biologically active protein domain with the fragment of an immunoglobulin. Antibody fusion proteins have the characteristics of antibodies and the activity of fusion functional proteins. According to the different Ig fragments bound, antibody fusion proteins can be divided into Fab fusion proteins, Fc fusion proteins, and single-chain antibody (scFv) fusion proteins. A BsAb is used to describe a large family of molecules designed to recognize two different epitopes or antigens. BsAbs come in many formats, ranging from relatively small proteins, which merely consist of two linked antigen-binding fragments, to large immunoglobulin G (IgG)-like molecules with additional domains attached. The different structures between BsAbs and fusion proteins are reflected in their molecular stability and clinical efficacy.

Treatment Paradigm for Pancreatic Cancer in China



Source: NHC, Diagnosis and treatment of pancreatic cancer (2018), Frost & Sullivan analysis

The following table sets forth features and limitations of 1L treatments for late-stage pancreatic patients.

Method	Features	Limitations
Chemo (e.g. mFOLFIRINOX, Gemcitabine + albumin-bound paclitaxel)	1. Recommended as the 1st line regimens in the NCCN Guideline. 2. Toxicity could be tolerated, especially the Gemcitabine + albumin-bound paclitaxel regimen.	1. The current ORR (5-11%) is still not satisfied, new mechanism for better efficacy is needed. 2. Drug resistance happens usually after one year treatment.TKI therapy may be less effective for patients with advanced liver disease. The guidelines only recommend the use of TKIs in patients with less severe sclerosis.
Anti-PD-L1/PD-1 antibody (e.g Pembrolizumab)	Broad-spectrum antitumor properties	High price, which imposes a huge financial burden on patients. Only useful in certain circumstance (if MSI-H, dMMR, orTMB-H [⩾10 mut/Mb])

Intended position and clinical focus of the Company's drug candidate

Treatment Paradigm for HCC

HCC Treatment Paradigm		
Systemic Therapy	Systemic chemotherapy	FOLFOX 4
	Molecular targeted drug	1L: Donafeni, Lenvartini, sorafenib
	Immunotherapy	First line: Anti-PD(L)1antibodies (Atezolizumab+bevacizumab, Sintilimab+bevacizumabanalogues) Second line: Regofinib*, Apatinib*, Karelizumab*, Tirelizumab*

Intended position and clinical focus of the Company's drug candidate

Source: NHC, Frost & Sullivan analysis

* Drugs that are not yet approved in China.

The following table sets forth features and limitations of treatments for late-stage HCC patients.

Method	Features	Limitations
Anti-PD-L1/PD-1 antibody (e.g. Atezolizumab)+anti-VEGF antibody (e.g. Bevacizumab)	1. Recommended as the 1st line regimens in the Guidelines, and better performance of Sorafenib. 2. Bevacizumab inhibits tumor angiogenesis, while further enhancing the ability of atelelizumab to restore the body's anti-cancer immunity by suppressing VEGF-related immunosuppression, promoting T-cell tumor infiltration, and initiating T-cell responses to tumor antigens.	1. The current ORR (20-30%) is still not satisfied, new mechanism for better efficacy is needed. 2. The choice of backline therapy is unclear when progression happens after this combination therapy
TKI (e.g. Sorafenib, Lenvatinib)	1. Recommended as the 1st line regimens in the Guidelines. 2. Sorafenib and lenvatinib are well tolerated.	1. The current ORR (5-11%) is still not satisfied, a new mechanism for better efficacy is needed. 2. Drug resistance happens usually after one-year of treatment. TKI therapy may be less effective for patients with advanced liver disease. The guidelines only recommend the use of TKIs in patients with less severe sclerosis.
Anti-PD-L1 antibody + Anti-CTLA-4 antibody	1. Recommended as the 1st line regimens in the NCCN Guideline. 2. CTLA-4 and PD-L1 inhibitor combination has shown additive antitumor activity associated with complementary immunostimulatory effects.	1. This regimen is approved only in USA. More clinical evidence may be required for an approval in other countries. 2. The side effects are severe and alerted by NCCN guidelines. 3. The current ORR (20%) is still not satisfied, new mechanism for better efficacy is needed.
Anti-PD-1 or PD-L1 antibody alone	Recommended as the 1st and 2nd line regimens in the Guidelines or in certain circumstances.	1. The current ORR (10-15%) is still not satisfied, new mechanism for better efficacy is required. 2. The application scenario is very limited. 3. The efficacy is noninferior to sorafenib as the 1st line regimens.

Intended position and clinical focus of the Company's drug candidate

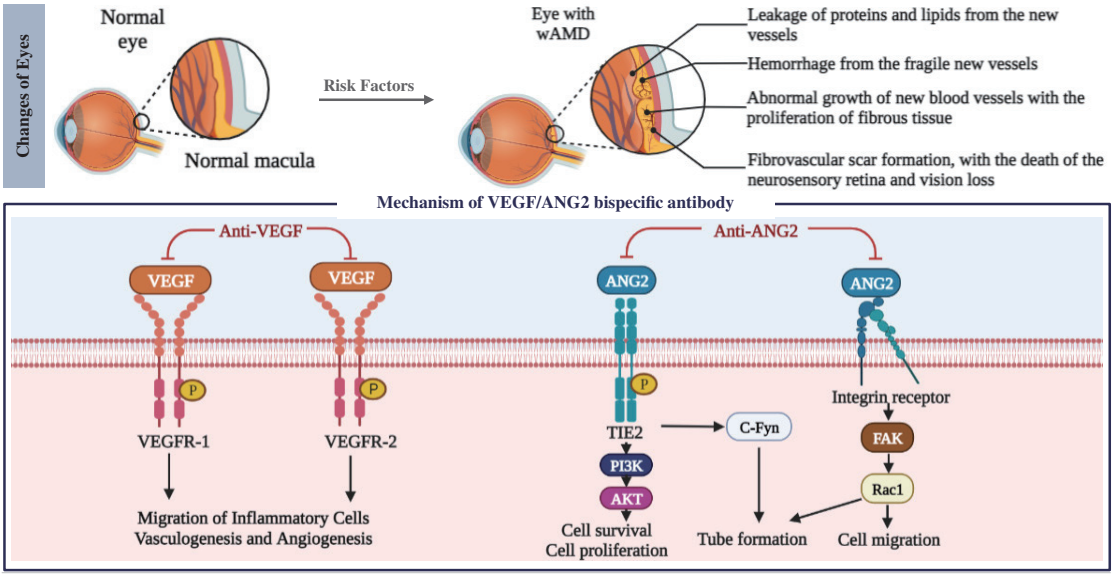
The development of combination therapy of PD-1 and TGF-β in cancer treatment is a validated therapeutic strategy. For instance, in 2021, Novartis AG completed a Phase I/Ib clinical trial of NIS793 (a TGF-β targeted mAb) in combination with PDR001 (a PD-1 mAb) in patients with advanced malignancies. Based on the results reported, NIS793 as single agent and in combination with PDR001 was effective in subjects with advanced malignancies. Such study identified new opportunities for the combination of PD-1 and TGF-β in cancer treatment. Encouraging efficacy results were also observed in the Phase I study of bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, in patients with pretreated biliary tract cancer, indicating the potential of PD-1/PD-L1 × TGF-β targeted monotherapies in treating solid tumors.

PD-L1 × TGF-β targeted combination therapies are under clinical development. The Phase Ib/II clinical trial of SHR-1701, a PD-L1 × TGF-β targeted fusion protein, in combination with gemcitabine and nab-paclitaxel has demonstrated the preliminary efficacy in treating patients with untreated locally advanced or metastatic pancreatic cancer. The CDE has also approved the Phase II/III clinical trial in China to evaluate the safety and clinical efficacy of SHR-1701 in combination with BP102 (biosimilar to bevacizumab) and XELOX in first-line treatment of patients with metastatic colorectal cancer, indicating the therapeutic potentials of PD-L1 × TGF-β BsAbs for metastatic colorectal cancer treatment.

VEGF × ANG2 TARGETED BISPECIFIC ANTIBODY MARKET

Mechanisms of VEGF × ANG2 Targeted BsAb

Vascular endothelial growth factor (VEGF) and angiopoietin-2 (ANG2) are important proteins functioning in vasculogenesis, angiogenesis and cell migration. Abnormal upregulation of those molecules causes inflammation and destabilizes the endothelial cell layer, which then leads to hypervascular permeability. The VEGF × ANG2 BsAb simultaneously binds to both VEGF and ANG2 and prevents the endothelial barrier from breakdown, which diminishes the symptoms of wet age-related macular degeneration (wAMD) and diabetic macular edema (DME). The diagram below illustrates the mechanism of action of the VEGF × ANG2 BsAb:



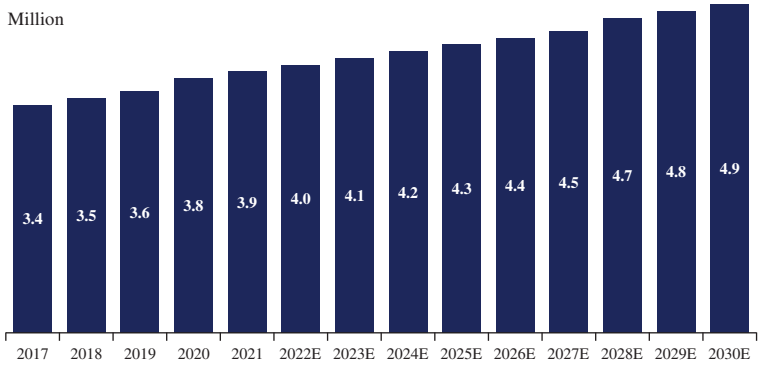
Source: Biomedicines. 2022 Aug 17;10(8):1996., Cells, 2019, 8(5): 471., Expert Opinion on Investigational Drugs, 2021, 30(3): 193-200., J Ophthalmol. 2012;2012:786870. Frost & Sullivan Analysis

China's Market of wAMD and DME Treatment

According to Frost & Sullivan, the simultaneous neutralization of VEGF and ANG2 has been envisioned as a novel candidate approach to wAMD and DME with better efficacy as a consequence of extended durability. The pool of wAMD and DME patients in China will steadily increase due to the growth of the aging population. From 2017 to 2021, the number of wAMD patients in China increased from 3.4 million to 3.9 million, representing a CAGR of 3.2%. It is estimated that wAMD patients in China will reach 4.3 million by 2025 and 4.9 million by 2030, representing a CAGR of 2.8% and 2.4%, respectively. The addressable wAMD patients of Y400, covers patients who are willing to receive treatment for wAMD. According to the White Paper of China Eye Health and Frost & Sullivan, the treatment rate for wAMD is approximate 70.0%, resulting in an estimated addressable wAMD patients of Y400 of 3.4 million in 2030 in China.

China's Prevalence of wAMD, 2017-2030E

Period	wAMD
2017-2021	3.2%
2021-2025E	2.8%
2025E-2030E	2.4%

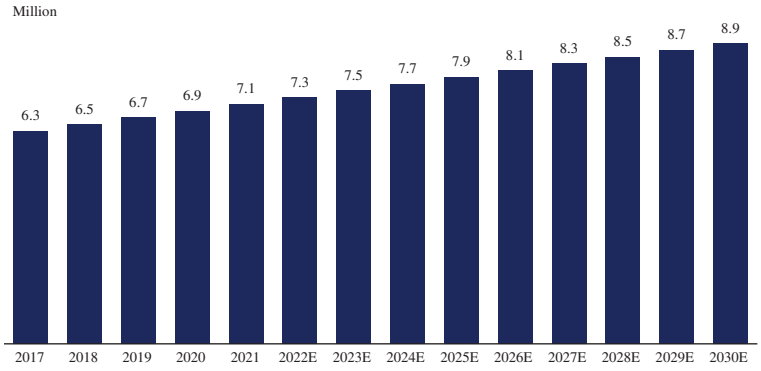


Source: NCCR, Frost & Sullivan analysis

From 2017 to 2021, the number of DME patients increased from 6.3 million to 7.1 million, representing a CAGR of 2.8%. It is estimated that DME patients in China will reach 7.9 million by 2025 and 8.9 million by 2030, representing a CAGR of 2.7% and 2.3%, respectively. The addressable DME patient of Y400, covers patients who are willing to receive treatment for DME. According to published research paper and Frost & Sullivan, the annual treatment rate for DME is approximate 30.0%, resulting in an addressable DME patients of Y400 of 2.7 million in 2030 in China.

China's Prevalence of DME, 2017-2030E

Period	CAGR
2021-2021	2.8%
2021-2025E	2.7%
2025E-2030E	2.3%

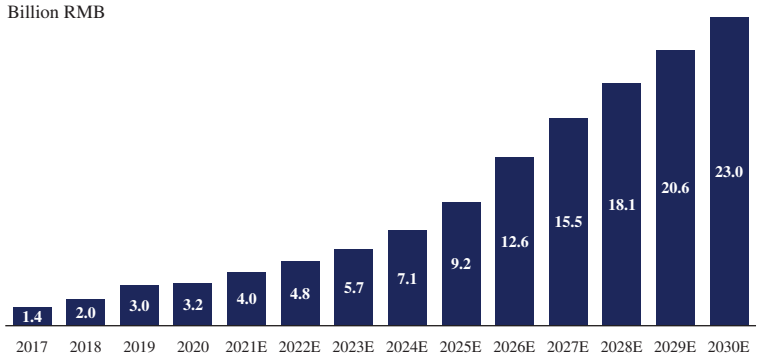


Source: NCCR, Frost & Sullivan Analysis

According to Frost & Sullivan, the market size of anti-VEGF mAb for retinal disease in China is experiencing a rapid growth. The market size of anti-VEGF mAb for retinal disease in China has grown from RMB1.4 billion in 2017 to RMB3.2 billion in 2020, with a CAGR of 32.7%. The market will keep growing to RMB9.2 billion in 2025 and RMB23.0 billion in 2030, with a CAGR of 23.8% and 20.1% respectively.

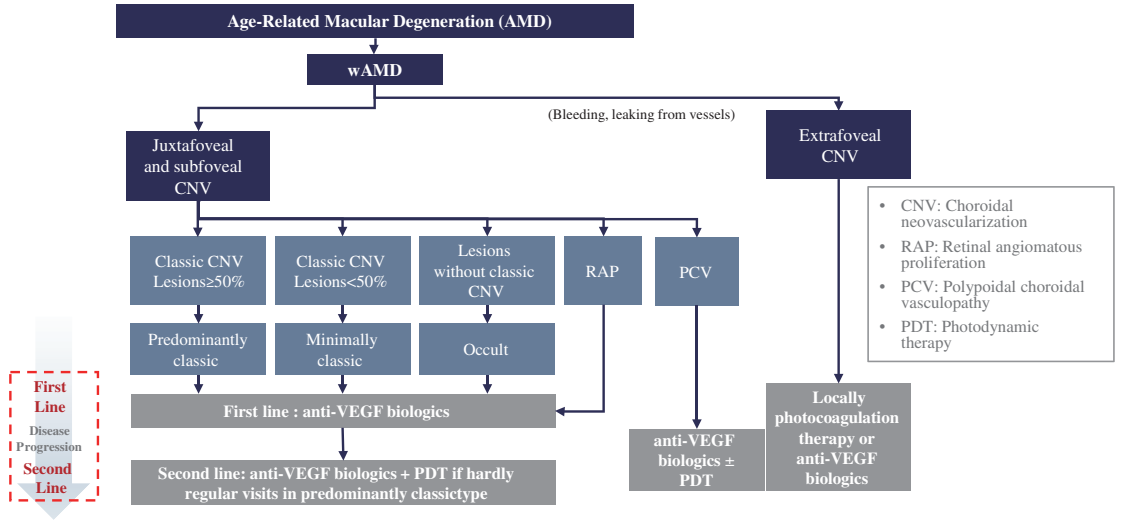
China Market Size of Anti-VEGF mAb for Retinal Diseases, 2017-2030E

Period	CAGR
2017-2020	32.7%
2020-2025E	23.8%
2025E-2030E	20.1%

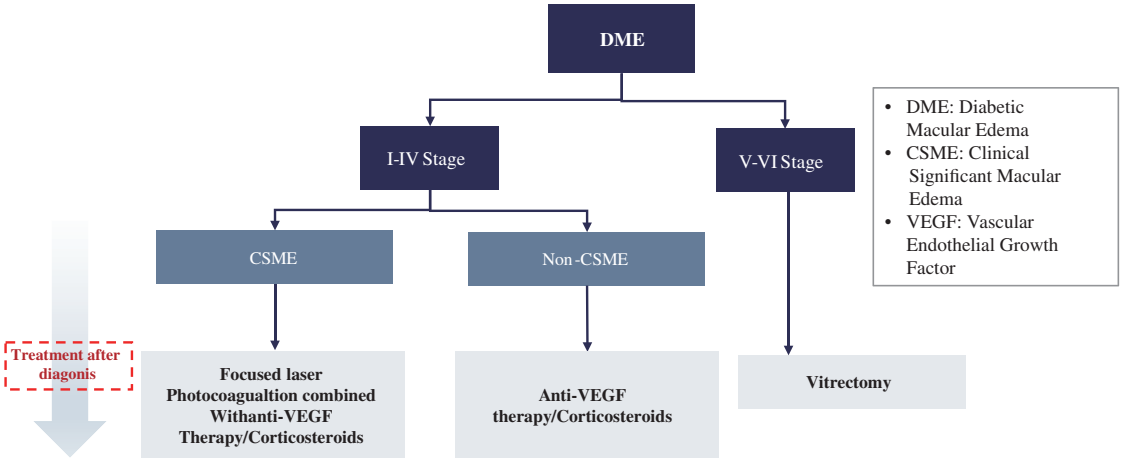


Source: Annual Reports of Listed Medical Companies, NCCR, MOHRSS, Frost & Sullivan Analysis

Treatment Paradigm for wAMD and DME in China and Globally



Source: CMA, Literature Review, Frost & Sullivan Analysis



Source: IDF, Frost & Sullivan Analysis

The following table sets forth features and limitations of treatments for wAMD and DME patients.

Major Treatments	Features	Limitations
photo-dynamic therapy, PDT	Making photosensitive drugs work under the action of laser. Destroying neovascularization and slowing down the rate of vision loss. The photosensitiser is first injected intravenously and then activated with a laser to close the neovascularisation using a photochemical effect. Combination with anti-VEGF antibodies can reduce the number of treatment.	Photosensitivity phenomenon causes the pain, swelling, bleeding or inflammation at the injection site. Used alone only for subtypes of typical subcentral sulcus choroidal neovascularization, with a small scope of application; Expensive photosensitizer (over RMB 10,000 per vial in China)
Laser Photocoagulation	Help patients with fundus disease avoid retinal detachment. Reduce the formation of new blood vessels in the eye; It is being phased out	Burning of vascular structures by a high-energy laser beam is only indicated for lesions far from the central macular recess. This may damage the nerve fibre layer and leave a dark spot in the visual field.
Hormone therapy	Vitreous cavity injection for the treatment of DME is the first treatment choice for DME in a few specific cases	Require repeated intraocular injections and poor patient compliance. The treatment causeintraocular hypertension and cataracts caused by the treatment
Anti-VEGF drugs	Significant improvement in neovascularization and endothelial cell proliferation. Reduced vascular permeability. The first treatment choice for wAMD and DME, for which the treatment has a more definitive effects and can significantly improve vision	VEGF mAbs require repeated intraocular injections which casuses infections and poor patient compliance. Some patients develop drug resistance after long-term anti-VEGF mAbs. Thus more efficient regimens targeting VEGF are needed.

Intended position and clinical focus of the Company's drug candidate

Competitive Landscape of wAMD and DME VEGF Targeted and ANG2 Targeted Drugs

As of the Latest Practicable Date, there were seven VEGF targeted antibody drugs or fusion proteins approved for the treatment of wAMD and DME globally (excluding China), at price ranging from US$783 per box to US$8,433 per box and three approved in China. VEGF targeted antibody drugs or fusion proteins can also be used in combination with other drugs, such as Dexamethasone, for the treatment of solid tumors.

The following table sets forth the details of the three marketed VEGF targeted antibody drugs or fusion proteins for the treatment of wAMD and DME in China as of the Latest Practicable Date:

China Marketed Drugs

Product	Drug Name	Developer	Target	Drug Type	Indication	Approval Date	Price (RMB) in 2021	Combination Therapy
Lucentis	Ranibizumab	Novartis Pharma Schweiz AG	VEGF	mAb	wAMD, DME	September 16, 2021	10mg/ml 0.2ml: 3,950	Combination with photodynamic therapy for wAMD
Lumitin	Conbercept Ophthalmic Injection	Chengdu Kanghong Biotechnology Co., Ltd.	VEGF	Fusion Protein	wAMD, DME, choroidal neovascularization and retinal vein occlusion secondary to macular edema	May 29, 2018	10mg/ml 0.2ml: 4,160	N/A
Eylea	Aflibercept Intravitreous Injection	Vetter Pharma-Fertigung GmbH & Co. KG	VEGF	Fusion Protein	wAMD, DME	February 2, 2018	40mg/ml 4mg: 4,100	Combination with subthreshold laser for diabetic macular edema treatment

Source: NMPA, Annual Reports of Listed Medical Companies, NRDL, Frost & Sullivan

As of the Latest Practicable Date, there were 56 and 15 VEGF targeted antibody or fusion protein drug candidates for the treatment of wAMD and DME under clinical development globally (excluding China) and in China, respectively. According to the CDE website, among the 15 VEGF targeted antibody or fusion protein drug candidate pipelines for wAMD and DME under clinical development in China, eight were in Phase III clinical trials, two were in Phase II clinical trials and five were in Phase I clinical trials. In addition to VEGF targeted antibody or fusion proteins, there are three drug candidates in China utilizing different methods in treating wAMD and DME under clinical development, including chemical drugs and gene treatments.

ANG2 is an important target for wAMD and DME treatment, for its possibly complementary or synergistic functions with other targets in tumor progressions. As of the Latest Practicable Date, only one ANG2 targeted antibody drug was approved for the treatment of wAMD and DME globally. As of the same date, there were seven and two ANG2 targeted antibody drug candidates or fusion proteins for the treatment of wAMD and DME under clinical development globally (excluding China) and in China, respectively. The following table sets forth the details of the one marketed ANG2 targeted drug globally as of the Latest Practicable Date:

Global Marketed Drugs

Product	Drug Name	Developer	Target	Drug Type	Indication	Approval Date	Price (USD)
VABYSMO	Faricimab	GENENTECH, INC.	VEGF, ANG2	BsAb	wAMD and DME	January 28, 2022	6mg/0.05ml 0.05ml: 2,315

Source: FDA, Annual Reports of Listed Medical Companies, Frost & Sullivan

The successful commercialization of VABYSMO evidenced the therapeutic potentials of VEGF × ANG2 BsAbs, including Y400, for treating wAMD and DME.

Among all the VEGF targeted drugs, VEGF × ANG2 drug candidates represent an emerging trend. As of the Latest Practicable Date, there were three VEGF × ANG2 drug candidates for treating neovascular eye diseases under clinical development in China:

China Pipeline

Product	Drug Name	Developer	Target	Drug Type	Indication	Highest Clinical Phase	First Posted Date[(1)]
Faricimab Injection	Faricimab	F. Hoffmann-La Roche Ltd	ANG2, VEGF	BsAb	DME, macular edema secondary to branch RVO, wAMD, CRVO or hemi retinal vein occlusion secondary to macular edema, polypoidal choroidal vasculopathy	III	2021/7/6
IBI324	IBI324	Innovent Biologics (Suzhou) Co. Ltd.	VEGF, ANG2	BsAb	DME	I	2022/6/17
ASKG-712	ASKG-712	Suzhou Aosaikang Biopharmaceutical Co., Ltd.	ANG2, VEGF	Fusion Protein	wAMD	I	2022/7/29

Source: NMPA, CDE, Frost & Sullivan Analysis

Abbreviations: RVO refers to retinal vein occlusion; CRVO refers to central retinal vein occlusion.

(1) "First Posted Date" in the context of China clinical trials refers to the date when the study corresponding to the highest clinical phase in China was first available on chinadrugtrials.org.cn after the Center for Drug Evaluation (CDE) has concluded its review. The CDE is an affiliated institution of the NMPA.

For a comparison of BsAbs and fusion proteins, please refer to the above section headed "Competitive Landscape of PD-1/PD-L1 × TGF-β Targeted Drugs".

As Y400 received the IND approval in April 2023, it's still at very early clinical development stage when compared to other VEGF targeted therapies and ANG2 targeted therapies, and face fierce competition for the treatment of wAMD and DME.

Future Trends and Needs of wAMD and DME Treatment

The future trends of wAMD and DME treatment mainly include: (a) an enlarged market size as wAMD's incidence increases with aging, and with the growth of the aging population in China, it is expected that wAMD patients in China will also grow and demand for effective treatment will increase; (b) the improved administration of drugs given the development of gene therapy in wAMD treatment, which allows patients to avoid eye injections and get more comfortable with alternative methods of administration; (c) the innovation of more durable treatments, since currently the intravitreal injection of anti-VEGF mAb drugs is inefficient in inhibiting angiogenesis, which calls for more durable drugs that could block both VEGF and other angiogenic factors; (d) the improved awareness of pre-clinical diagnosis of DME, which allows early detection and treatment; (e) the development of combination therapies that can reduce the incidence of certain complications of DME; and (f) the introduction of innovative therapies that have higher efficacy, while reducing patient discomfort, thereby improving patient compliance.

Despite the continuous development of therapies to address the demands of wAMD and DME patients, there remain medical demands, including the following: (a) intraocular injections of anti-VEGF drugs require frequent injections to have a good therapeutic effect, but frequent dosing can impose a financial burden to the patients; (b) photodynamic therapy (PDT) may result in inadequate choroidal perfusion, which is a significant inflammatory response at the treated site and increased VEGF expression, with a risk of compromising long-term visual prognosis and a high recurrence rate; (c) in addition to overcoming fear with each injection, patients also face the risk of infection due to frequent injections, and anti-VEGF therapy has limited effect on reducing the inflammation that leads to wAMD; (d) the inconvenience of drug administration, as most drugs are given by eye injection, which lack durability and intensifies inconvenience. Additionally, wAMD patients need to have eye injections every one or two months, which leads to low patient compliance; (e) the inefficiency of the intravitreal injection of VEGF drugs, since single-target VEGF inhibitors promote the upregulation of other angiogenic factors, which impairs the efficacy of treatment; and (f) difficulties of diagnosis, as few symptoms of DME could be diagnosed in the early stages, and since DME is a common complication of diabetes, its treatments are often associated with diabetic medicines, which have known adverse effects such as headaches and drug resistance.

VEGF × TGF-β TARGETED BISPECIFIC ANTIBODY MARKET

VEGF is a growth factor overexpressed in most solid tumors and a key driver of angiogenesis, the process that leads to the formation of new blood vessels within and around tumors. In addition to stimulating tumor angiogenesis, VEGF plays a negative role in tumor immunity via various mechanisms within the TME. TGF-β also negatively regulates multiple immune cells, facilitates the generation of CAF and stimulates the EMT process of tumor cells that restricts T cell infiltration.

As of the Latest Practicable Date, no VEGF × TGF-β targeted drugs were marketed either globally or in China. As of the same date, one VEGF × TGF-β targeted BsAb and one PD-L1 × VEGF × TGF-β fusion protein were under clinical trials globally.

Global Pipeline

Product	Developer	Target	Drug Type	Indication	Highest Clinical Phase		First Posted Date[(1)]
PM8003	Biotheus Inc.	PD-L1, VEGF, TGF-β	Fusion protein	Advanced Solid Tumor	China	I	2021/7/30
ZGGS18	Suzhou Zelgen Biopharmaceuticals Co., Ltd..	VEGF, TGF-β	BsAb	Advanced Solid Tumor	Global China	FDA IND Approval I/II	\ 2022/10/20

Source: NMPA, CDE, FDA, Frost & Sullivan Analysis

(1) "First Posted Date" in terms of global clinical trials refers to the date when the study corresponding to the global highest clinical phase (except China) was first available on ClinicalTrials.gov after the National Library of Medicine has concluded its quality control review; "First Posted Date" in the context of China clinical trials refers to the date when the study corresponding to the highest clinical phase in China was first available on chinadrugtrials.org.cn after the Center for Drug Evaluation (CDE) has concluded its review. The CDE is an affiliated institution of the NMPA.

For a comparison of BsAbs and fusion protein, please refer to the above section headed "Competitive Landscape of PD-1/PD-L1 × TGF-β Targeted Drugs".

Both the TGF-β and VEGF pathways are the representative pathways of the innate anti-PD-1 resistance signatures, related to immunosuppressive processes. Therapeutic agents targeting TGF-β and VEGF, may synergize with existing immunotherapies to overcome immune checkpoint blockade resistance, indicating great therapeutic potentials of TGF-β targeted drugs for solid tumor treatment. The combination of PD-1 and TGF-β in cancer treatment have been clinically validated. For instance, Avastin (bevacizumab), a VEGF targeted mAb, is approved to treat several solid tumors, including metastatic colorectal cancer, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, relapsed glioblastoma, hepatocellular carcinoma, metastatic HER2-negative breast cancer, epithelial ovarian cancer, fallopian tube cancer or primary peritoneal cancer and cervical cancer.

CHINA'S COVID-19 VACCINE MARKET

Overview

The COVID-19 pandemic is an ongoing public health crisis caused by infections and spread of the severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2. Recent mutated variants of the virus have emerged, some are more aggressive and infectious. According to the World Health Organization, until November 28, 2022, there were 637 million confirmed COVID-19 cases and over 6.6 million related deaths worldwide. After a brief rebound in 2021, the new variants of the COVID-19 virus, among other factors, have caused a significant slowdown of the global economy in 2022. In response to the COVID-19 pandemic, the international community has continued to concentrate research and development efforts on combating the pandemic, and ensure global access to diagnostic equipment, therapies, vaccines and other resources.

Types of COVID-19 Vaccines

COVID-19 vaccines are developed using a number of classic and innovative technologies, of which four technology routes have generated approved products: inactivated vaccine, recombinant subunit protein vaccine, viral vector vaccine and nucleic acid vaccine. These technology routes have different benefits and limitations in terms of safety, efficacy, supply and storage conditions, and therefore are suitable to different population segments with different vaccination history and needs, immunity conditions and technology preferences. When compared to other technology routes, the recombinant subunit protein vaccine is safe and effective, represents an established technical pathway, and could achieve scalable manufacturing.

Main Technical Classification of COVID-19 Vaccines

	Mechanism	Advantage	Limitation
Inactivated Vaccine	Use killed pathogen to induce the production of antibodies	Established technical pathway; Quick and scalable manufacturing; Effective;	Large dose; May cause antibody-dependent enhancement (ADE);
Recombinant Subunit Protein Vaccine	Use the spike (S) protein of SARS-CoV-2 as the antigen to induce the production of antibodies	Safe and effective; Established technical pathway; Scalable manufacturing;	Antigenicity subject to the expression system
Viral Vector Vaccine	Use viral vector that cause no harm to human body to carry the gene of the spike (S) protein into the body, and produce the spike (S) protein to trigger production of antibodies	Safe and effective; Few side effects; Easy administration and less doses taken;	Long R&D process; May have pre-existing immunity (has infected with the vector virus before so that there are neutralizing antibodies against the vector virus in the body)
Nucleic Acid Vaccine	Direct injection of the gene of the spike (S) protein, use human cell to produce antigen and then trigger production of antibodies	No need to express protein or virus during manufacturing; Safe	Scalable manufacturing process need optimization; mRNA is not stable; Difficult for the vaccine to enter cells

Source: WHO, CDC, Chavda, V. P., Hossain, M. K., Beladiya, J., & Apostolopoulos, V. (2021). Nucleic acid vaccines for COVID-19: a paradigm shift in the vaccine development arena. Biologics, 1(3), 337-356.;Heidary, M., Kaviar, V. H., Shirani, M., Ghanavati, R., Motahar, M., Sholeh, M., Ghahramanpour, H., & Khoshnood, S. (2022). A Comprehensive Review of the Protein Subunit Vaccines Against COVID-19. Frontiers in microbiology, 13, 927306. https://doi.org/10.3389/fmicb.2022.927306; Vanaparthy, R., Mohan, G., Vasireddy, D., & Atluri, P. (2021). Review of COVID-19 viral vector-based vaccines and COVID-19 variants. Le infezioni in medicina, 29(3), 328 -338. https://doi.org/10.53854/liim-2903-3; Khoshnood, S., Arshadi, M., Akrami, S., Koupaei, M., Ghahramanpour, H., Shariati, A., ... & Heidary, M. (2022). An overview on inactivated and liveattenuated SARS-CoV-2 vaccines. Journal of Clinical Laboratory Analysis, 36(5), e24418.

Demand for COVID-19 Vaccines

Different variants of the SARS-CoV-2 virus have emerged and are circulating globally including in China. New information about the characteristics of these variants is rapidly emerging, and there is a growing public awareness of the necessity to receive vaccination against emerging variant strains. As a result, additional boosting might be required because of waning immunity to the primary vaccination. Some recent studies have shown that the antibody concentration declined in the third month after administration of two doses of inactivated vaccines, and the protection rate of currently approved mRNA vaccines declined to approximately 40% in six months. These indicate a significantly larger and longer-term market demand for booster shots and re-vaccination of COVID-19 vaccines.

There is a global shortage of COVID-19 vaccines which is caused by the limited supply capacity as compared to the vast global population to be vaccinated and uneven access to COVID-19 vaccines among nations. As of December 31, 2021, the vaccination rate in China and globally were 51.2% and 57.2%, respectively. From March 23, 2021 to December 31, 2021, the total COVID-19 vaccine doses administered in China and globally were 2.8 billion and 39.7 billion, respectively. While COVID-19 continues to spread and as new variants emerge in countries without access to adequate supply of COVID-19 vaccines, there is a huge market gap that needs to be met urgently in order to achieve herd immunity against COVID-19 globally.

Competitive Landscape of COVID-19 Vaccines in China and Globally

As of the Latest Practicable Date, 15 COVID-19 vaccines had received marketing approvals in the PRC, consisting of five inactivated vaccines, three recombinant adenovirus viral vector-based, six recombinant subunit protein vaccines and one mRNA vaccine. As of the same date, 32 clinical-stage COVID-19 pipeline candidates in the PRC were being developed, including nine using the recombinant subunit protein route, according to the CDE and WHO websites.

Additionally, as of the Latest Practicable Date, 58 COVID-19 vaccines had received marketing approvals globally, consisting of 13 inactivated vaccines, 12 recombinant adenovirus viral vector-based, 22 recombinant subunit protein vaccines, 11 nucleic acid vaccines, and 242 clinical-stage COVID-19 pipeline candidates were being developed globally, of which 79 were using the recombinant subunit protein route, according to the CDE and WHO websites.

Competitive Landscape of Marketed COVID-19 Vaccines in China

The chart below illustrates the marketed COVID-19 vaccines in China as of the Latest Practicable Date.

Product Name	Company	Technology	Route of Administration	Dosages Per Year	Approval Time	Efficacy/duration of Protection against Different Variants
科维福	Institute of Medical Biology, Chinese Academy of Medical Sciences	Inactivated Vaccine	Intramuscular injection	2	6/9/2021	Good safety and immunogenicity had the ability to cross-neutralize against the new crown strain from
克尔来福 (CoronaVac)	Beijing Kexing Zhongwei Biotechnology Co., Ltd.	Inactivated Vaccine	Intramuscular injection	2	2/5/2021	The interim analysis in Turkey was able to achieve a protection rate of 91.25%, and the results of the phase III clinical study in Indonesia have been published, with a protection rate of 65.3%. The protection rate for medical visits reached 78%. The overall protection rate for health care workers in high-risk groups is also 50.3%.
可维克 (KCONVAC)	Shenzhen Kangtai Biological Products Co.,Ltd.	Inactivated Vaccine	Intramuscular injection	2	5/14/2021	The geometric mean titer (GMT) of live virus neutralizing antibody in the 0-28 day immunization program vaccine group in the phase I and II clinical trials of this vaccine was 131.7, which was 2.65 times higher than the GMT of 49.7 in serum neutralizing antibody in recovered patients. According to the data from the phase I/II clinical trial of Kangtai Bio New Crown vaccine, the vaccine did not cause any serious adverse reactions of grade 3 or above, and the overall incidence of adverse reactions was not significantly different compared with the placebo group.
众康可维 (WIBP-CorV)	Wuhan Biological Products Research Institute Co., Ltd.	Inactivated Vaccine	Intramuscular injection	2	2/5/2021	JAMA journal published online the data of the phase III clinical interim detailed analysis of two inactivated new crown vaccines from Beijing Institute and Wuhan Institute, a subsidiary of Sinopharm China Biological Group. The results showed that the vaccine efficacy was 78.1% for Zongaikovi compared to using only aluminum adjuvant alone.
众爱可维 (BBIBP-CorV)	Beijing Institute of Biological products CO., LTD	Inactivated Vaccine	Intramuscular injection	2	12/30/2020	JAMA journal published online the data of the phase III clinical interim detailed analysis of two inactivated new crown vaccines from Beijing Institute and Wuhan Institute, a subsidiary of Sinopharm China Biological Group. The results showed that the vaccine efficacy was 72.8% for Zongkangkovi compared to using only aluminum adjuvant alone.
智克威得	Anhui Zhifei Longcom Biopharmaceutical Co.,Ltd	Recombinant Subunit Protein Vaccine (CHO Cell)	Intramuscular injection	3	3/1/2022	Published in the New England Journal of Medicine, the world's top academic journal, clinical results showed that the vaccine was 81.4% effective in preventing any severity of NCCP in subjects who completed the full course of vaccination, and remained 75.7% effective in preventing any severity of NCCP in a long-term effectiveness analysis 6 months after the full course of vaccination.
克威莎 (肌注式)	Cansino Biologics Inc.	Viral Vector Vaccine	Intramuscular injection	1	2/25/2021	Journal of Emerging Microorganisms and Infections: Preclinical results show that the novel coronavirus mRNA vaccine from Concepcion Biologics has strong immune protection against different new coronavirus variants. Two doses of mRNA-Beta induced broad protection against both the original strain and the Beta variant. At the same time, the use of mRNA-Omicron as a booster, either homologous booster for mRNA-Beta or heterologous sequential booster for Convivox's new recombinant coronavirus vaccine Kvisa, significantly increased the level of neutralizing antibodies against the four strains, especially against the Omicron variant, providing durable and efficient protection
克威莎 (肌注式)	Cansino Biologics Inc.	Viral Vector Vaccine	Inhalation	1	3/1/2021	Immunogenicity results showed that after 28 days of sequential booster immunization with inhalation kvassa, neutralizing antibody levels against the original strain were 18.4-26.4 times higher in the two dose groups than in the inactivated homologous booster group (GMT 1937.3 in the low dose group, GMT 1350.8 in the high dose group, and GMT 73.5 in the inactivated homologous booster group). Also, sequential booster inhalation Neocrown vaccine had high levels of cross-protection against delta mutant strains, with 18.1-24-fold higher levels of neutralizing antibodies than inactivated vaccine. Inhalation kwashiorkor also efficiently induced mucosal immunity. The results of RBD-specific IgA conjugated antibody levels in serum of subjects within 28 days after booster immunization showed that IgA levels of sequential booster inhaled Neocrown vaccine were significantly higher than those of inactivated vaccine homologous booster, with GMT 114.3 in the low-dose group, GMT 116.3 in the high-dose group and GMT 11.2 in the inactivated homologous booster group
丽康V-01	Lizhu Pharmaceutical Group Co., Joincare Pharmaceutical Group Industry Co., Ltd.	Recombinant Subunit Protein Vaccine (CHO Cell)	Intramuscular injection	1	9/14/2022	The absolute protection rate is 61.35% with the sequential booster of Likang V-01 on top of the two inactivated vaccines, including 61.19% for the high-risk group (people over 60 years old or with underlying diseases) and 71.83% for people with underlying diseases. In terms of safety, the safety of Likang V-01 is significantly better than that of mRNA vaccine and adenovirus vaccine. Most of the adverse events (AEs) were mild, with recruitment AEs (injection site pain, headache, fatigue, fever, non-vaccination site muscle pain) data significantly lower than those of the mRNA vaccine, which can provide safer protection.
SCTV01C	Sinocelltech Group Limited	Recombinant Subunit Protein Vaccine	Intramuscular injection	1	12/4/2022 (emergency use)	The results of three completed clinical studies showed that SCTV01C exhibited outstanding immunopersistence after immunization.
威克欣	WestVac Biopharma Co.,Ltd, West China Hospital of Sichuan University	Recombinant Subunit Protein Vaccine (Sf9 Cell)	Intramuscular injection	3	12/2/2022 (emergency use)	Both the BA.1 and BA.5 variants of the currently prevalent Omicron strains induced uniformly high neutralizing antibody titers against the true virus. In addition, booster immunization with SCTV01C maintained high neutralizing antibody titers in the range of 170-678 at 12 months, demonstrating the outstanding immune durability of SCTV01C.
SCB-2019	Sichuan Clover Biopharmaceuticals Co., Ltd., GlaxoSmithKline Pharmaceuticals	Recombinant Subunit Protein Vaccine (CHO Cell)	Intramuscular injection	2	12/5/2022 (emergency use)	New phase III data demonstrating broad-spectrum neutralization – including against the globally dominant subtype of Omicron BA.5 variant – underscore the potential role of SCB-2019 (CpG 1018/aluminum adjuvant) as a universal booster in China and other countries, regardless of prior vaccination route or history of infection, and for different age groups.
DelNS1-2019-nCoV-RBD-OPT1	Beijing Wantai Biological Pharmaceutical Co.	Viral Vector Vaccine	Nasal spray drug delivery	2	12/5/2022 (emergency use)	Induction of strong innate and acquired local immune responses in the respiratory tract, rapid (24-hour onset of action), durable and broad protection against SARS-CoV-2 attack in hamsters, even when administered 24 hours after SARS-CoV-2 infection. Nine months after vaccination with two doses of dNS1-RBD, the protection provided by vaccination against the SARS-CoV-2 beta variant remained as good as that against the original virus strain.
SCTV01E	Sinocelltech Group Limited	Recombinant Subunit Protein Vaccine	Intramuscular injection	1	3/23/2023 (emergency use)	It is showed that during the epidemic of Omicron BA.5, B.7 and XBB variants in China, SCTV01E produced good protective efficacy against Omicron and its variants with good safety after one dose of enhanced immunization in people ≥18 years of age who had completed basic or enhanced immunization against COVID-19 vaccine. The Phase III clinical study also observed for the first time the protective efficacy of COVID-19 vaccine against asymptomatic infection, with the protective efficacy of 100% and 42.9% for asymptomatic patients 14 and 7 days after vaccination, respectively.
SYS6006	CSPC Pharmaceutical Group	mRNA	Intramuscular injection	1	3/22/2023 (emergency use)	After receiving one booster dose of SYS6006, the geometric mean titers of neutralizing antibodies (GMT) against Omicron BA.5 was 236, which is 83 times higher than before the booster shot was given. For those who received either 2 or 3 doses of the inactivated vaccine, the sequential boosting immunization with one dose of SYS6006 showed cross-neutralizing effects against strains such as Omicron BA.5, BF.7, BQ.1.1, XBB.1.5, and CH.1.1.

Source: NMPA, CDE, FDA, WHO, Medicine Instructions, Clinical Trials, Frost & Sullivan

Competitive Landscape of Recombinant Subunit Protein COVID-19 Vaccines in China

As of the Latest Practicable Date, there were nine recombinant subunit protein COVID-19 vaccines in China under clinical development, including Y2019. The chart below illustrates the marketed recombinant subunit protein COVID-19 vaccines under development in China as of the Latest Practicable Date:

China Marketed Products

Product	Company	Medicine	Indication	Approval Time
智克威得	Anhui Zhifei Longcom Biopharmaceutical Co.,Ltd	Recombinant Subunit Protein Vaccine(CHO Cell)	COVID-19	2022/3/1
麗康V-01	Lizhu Pharmaceutical Group Co., JoincarePharmaceutical Group Industry Co., Ltd.	Recombinant Subunit Protein Vaccine (CHO Cell)	COVID-19	2022/9/14
SCTV01C	Sinocelltech Group Limited	Recombinant Subunit Protein Vaccine	COVID-19	2022/12/4 (for emergency use)
威克欣	WestVac Biopharma Co.,Ltd, West China Hospital of Sichuan University	Recombinant Subunit Protein Vaccine (Sf9 Cell)	COVID-19	2022/12/2 (for emergency use)
SCB-2019	Sichuan Clover Biopharmaceuticals Co., Ltd., GlaxoSmithKline Pharmaceuticals	Recombinant Subunit Protein Vaccine (CHO Cell)	COVID-19	2022/12/5 (for emergency use)

Source: Annual Reports of Listed Medical Companies, NMPA, CDE, Frost & Sullivan Analysis

(1) "First Posted Date" in the context of China clinical trials refers to the date when the study corresponding to the highest clinical phase in China was first available on chinadrugtrials.org.cn after the Center for Drug Evaluation (CDE) has concluded its review. The CDE is an affiliated institution of the NMPA.

The successful commercialization of the six recombinant subunit protein COVID-19 vaccines in China evidenced the great therapeutic potentials of recombinant subunit protein vaccines against SARS-CoV-2 and its VOCs.

REPORT COMMISSIONED BY FROST & SULLIVAN

In connection with the [**REDACTED**], we have engaged Frost & Sullivan to conduct a detailed analysis and prepare an industry report on the worldwide and China market. Frost & Sullivan is an independent global market research and consulting company which was founded in 1961 and is based in the United States. Services provided by Frost & Sullivan include market assessments, competitive benchmarking and strategic and market planning for a variety of industries. The contract sum to Frost & Sullivan is RMB900,000 for the preparation of the Frost & Sullivan Report. 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 biologics market for potential investors. 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's may be affected by the accuracy of these assumptions and the choice of these primary and secondary sources.